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EFFECT OF RADIOPROTECTIVE AGENTS ON REACTIVITY TO SPACE FLIGHT FACTORS

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[Article by Ye. I. Vorob'yev, V. I. Yefimov and S. K. Karsanova]

[English abstract from source] The review summarizes and discusses the experimental and clinical data published during the last 15 years that concern the effect of radioprotectors on the reactivity of organisms exposed to acceleration, vibration, motion sickness, hypodynamics, hypo- and hyperoxia.

[Text] During manned space flights it is imperative to consider the fact that the cosmonaut is exposed to the complex effects of several factors in the most varied combinations. This circumstance determined the urgency of studying not only the combined effect of radiation and other extreme environmental and space flight factors [1-4], but distinctions of effects on the body of radioprotective agents (radioprotectors) against the background of altered reactivity.

We have tried to analyze and summarize data from the literature and results of clinical and physiological studies of man dealing with modification of a number of extreme space flight factors by means of various radioprotective agents.

Long-term accelerations (G forces): There are many studies dealing with the influence of protective agents on the physiological effects of transverse and longitudinal accelerations. The very first of these studies raised the question of animal endurance of accelerations after being given radioprotectors, with reference to the prospects of pharmacological protection during space flights [5]. The very earliest works in this direction revealed that certain thiol (cystamine, cysteamine, cystaphos, aminoethylisothiuronium--AET), as well as amine (mexamine, serotonin) protectors diminishes mouse and guinea pig resistance to accelerations. True, the changes in resistance were phasic [2, 6, 7]. In subsequent studies, it was shown that the nature of the effects of protectors on resistance depends on dosage thereof, force and time of exposure to accelerations, as well as species of animal. For example, when mice were given thiolprotectors a few minutes before accelerations there was a decrease in resistance for the first 30 min. Resistance to back-chest accelerations reverted to normal 2-4 h after giving cystamine in a dosage of 50-100 mg/kg. But with a dosage of 150 mg/kg, this occurred only after 24 h.

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*This issue is dedicated to the bright memory of Avetik Ignat'yevich Burnazyan.

Cystaphos and AET had analogous effects, but somewhat "softer" than cystamine [8, 9]. V. A. Kozlov and B. I. Davydov [10], who conducted experiments on guinea pigs given cystamine, AET or β-mercaptopropylamine, demonstrated that with exposure to accelerations at 15-min intervals these animals developed decompensation of cardiac function faster and more severely than control animals. S. L. Freydman observed a decrease in resistance to chest-back accelerations in rabbits also under the influence of cystamine (10 and 70 mg/kg) and cystaphos (15 and 100 mg/kg) [11, 12]. At the same time, V. I. Generalov [13, 14] and A. V. Pastushenkov [15] described an increase in tolerance of head-pelvis accelerations by mice and rats 15 min after being given cystamine (100-200 mg/kg) or its derivatives. According to the data of N. N. Dobrov et al. [16], a mixture consisting of cystamine, phenamine and epinephrine did not have an adverse effect on animal endurance of accelerations.

In the opinion of some researchers [2, 17-19], there is apparently potentiation of the hypoxic effect in vital organs under the combined influence of radioprotectors and accelerations. There is faster expenditure of energy materials (in particular, glycogen). The possibility cannot be ruled out that administration of protectors, which aggravates hypoxia, elicits depletion of reserve mechanisms and breakdown of compensation, which is apparently the basis for diminished resistance to accelerations. According to the data in [20], 2-fold exposure of mice to accelerations led to a reduction in average size of hepatocyte nuclei, which persisted for up to 5 months. Administration of the radioprotector, dibromohydrate bis-(2-aminoethyl) disulfide prior to accelerations increased even more the number of cells with reduced nuclei which, in the authors' opinion, is indicative of diminished resistance to accelerations after administration of this sulfur-containing protective agent.

S. L. Freydman and A. N. Khlebnikov, who tested the effects of serotonin and mexamine on metabolism of rats and rabbits exposed to 12-unit accelerations, demonstrated that both protective agents in doses of 20 mg/kg aggravated hypoxia. But preventive administration of these protectors in a dosage of 1 mg/kg improved significantly animal resistance to accelerations [21, 22]. There have been previous reports of improved resistance of mice and rats to head-pelvis accelerations by giving them certain antihypoxants (all of which were thiuronium compounds) [15, 23-25]. Of the agents used, guianylthioureia (gutimin) was the most effective. Yet this compound is a radioprotector that elicits a moderate protective effect [26]. Similar results were obtained by other authors who tested the effects of gutimin [27, 28]. The radioprotector amygdalin had an analogous effect, when given preventively to mice (20 mg/kg) and rabbits (50 mg/kg). Amygdalin did not have an appreciable effect on resistance of rats to accelerations. Large doses of this product diminished resistance of all animals to accelerations [29].

Studies of animal reactivity in the aftereffect period following exposure to transverse accelerations revealed a number of phasic changes in sensitivity to toxic doses of cystamine, AET, cystaphos and mexamine. The nature and degree of sensitivity depended on magnitude of accelerations and product. For example, unlike thiol protectors, heightened resistance to mexamine persisted from the first minutes after administration for 24 h [30-33].

Several studies were concerned with the reactions to accelerations of irradiated animals given various protectors. For example, B. I. Davydov [34], who exposed mice to radiation in doses of 500-400 R 2-40 days after giving them cystamine,

cystaphos, mexamine or serotonin, and exposed them to accelerations. The protected animals presented a biphasic reaction to accelerations: increased resistance was observed for the first 2-5 days, and this was followed by a decrease. The dynamics of resistance to accelerations resembled those observed with irradiation without protection. At the stage of postradiation recovery, the author observed, radioprotectors had an insignificant effect on reactivity to accelerations of animals who survived after irradiation. An important conclusion was derived [16] to the effect that giving radioprotectors prior to exposure to the combination of radiation and accelerations (a radioprotective mixture of cystamine, phenamine and epinephrine was used) not only increased animal survival rate, but decreased the period of half-recovery of radioresistance.

There were less marked pathomorphological changes in hemopoietic organs of animals exposed to 700 R radiation after administration of cystamine and AET, who were submitted to accelerations 24 h prior to this [18]. S. N. Mozharov [35] described the manifestation of the protective effect of a combination of these protectors, which was demonstrated on the basis of rate of recovery processes in the innervation system of muscles of mice submitted to accelerations after irradiation. Use of cystamine hydrobromide with a combination of accelerations and irradiation caused faster and fuller recovery of damaged tissues [19]. A radioprotective effect was also demonstrated in the liver and gonads of rat and mice given bis-(2-aminoethyl) disulfide dihydrobromide in cases of two-fold exposure to accelerations and repeated irradiation [36, 37].

Studies have been made of long-term (after 13 months) status of mice exposed to 5-fold radiation in a total dosage of 1020 R within 3 months and 2-fold exposure to accelerations at an interval of 90 days [38, 39]. The animals were given cystamine prior to the second and fourth irradiation, and the anterior third of the abdomen was shielded during second, third and fourth exposure to radiation. In protected animals, cystamine limited the severity of changes in the liver, spleen, as well as diaphragma. The least changes were noted in mice given this protector and with shielding of the abdomen. It has been reported that animal resistance to accelerations increased after giving them the adaptogen, eleuterococcus [40-42]. Eleuterococcus enhanced not only radioresistance, but resistance to repeated accelerations after irradiation [43, 44].

Of special significance are clinical studies of man's endurance of prolonged accelerations after intake of radioprotective agents. The radioprotector ambratin--cysteamine hydrotartrate with pyridoxine--has been studied in this aspect [45]. Intake of ambratin by mouth had no appreciable adverse effect on human endurance of prolonged chest-back or head-pelvis accelerations [46].

Vibration: This dynamic factor, like prolonged accelerations, can modify the body's reaction to radiation. Like accelerations (though less distinctly), vibration slows down postradiation recovery [47]. There has been little coverage in the literature of modification by this factor of the effects of radioprotection. V. A. Kozlov et al. [48] discovered that mice developed heightened sensitivity to cystamine (true, not significantly) after exposure to total-body vibration. At the same time, according to P. P. Saksonov et al. [2], there was full expression of the protective effect of cystamine against radiation (experiments on mice and rats) even after prior exposure to vibration. These authors observed that occasionally the efficacy of the protector in the case of combined factors even exceeded its effect in the case of ionizing radiation alone.

Vestibular analyzer. Motion sickness: The human vestibular analyzer functions under unusual conditions during space flights. The occurrence of inflight vestibulovegetative reversible disorders, similar to motion sickness and impairment of spatial orientation (set of symptoms of motion sickness) is based on altered gravity and related to impaired analyzer function. Other flight factors, including ionizing radiation, may also cause vestibulovegetative disorders. Marked changes can occur in both threshold sensitivity and reactivity of the vestibular analyzer under the influence of even relatively low doses of radiation (50 R) [49].

Several studies dealt with the functional state of the vestibular analyzer after giving radioprotective agents, considering its nonspecific "vulnerability" during flights. Thus, there have been reports of studies of the rabbit vestibular analyzer after intake of ambratin, mexamine and amitetravit [50, 51]. The last mentioned agent is a vitamin and amino acid complex, a protector with biological action and an adaptogen [52]. It has been established that none of the tested protectors aggravate manifestation in the animals of vestibulosomatic and vestibulovegetative reactions. Mexamine given against ionizing radiation (500 R) provided protection of the analyzer, causing faster normalization of its threshold sensitivity and reactivity than in the control. P. I. Kumets [53] studied the canine vestibular analyzer during long-term chronic irradiation for 3 years combined with subacute irradiation 3 times a year (cumulative dose in 3 years 560 rad). According to his data, therapeutic and preventive measures used during the irradiation period, in the form of periodic administration of amitetravit and ATP, attenuated significantly the deleterious effect of ionizing radiation on the vestibular analyzer. The vestibulometric reactions of protected dogs resembled those of intact (nonirradiated) animals.

Studies of labyrinthine reactions of healthy people under clinical conditions after intake of ambratin, mexamine or amitetravit revealed that none of the protective agents had a toxic effect on the vestibular analyzer in the tested doses at the time of their maximum concentration in blood (after 0.5-2.5 h). They also had no appreciable adverse effect on human resistance to cumulative Coriolis accelerations (CCA). Enhancement of vestibular resistance of man after intake of amitetravit for 2 weeks merits attention. In this case, resistance to CCA had a tendency to persist for 6-8 days [51, 54]. N. Ya. Lukomskaya and M. I. Nikol'skaya showed that in people extremely sensitive to seasickness the efficacy of eleuterococcus constituted 81% of the efficacy of scopolamine (1 mg/kg), considered to be 100%. The protection index of eleuterococcus was even higher than that of ethaperazine [55]. According to the findings of Ye. F. Baburin et al. [56, 57], intake of eleuterococcus extract enhanced endurance of CCA during passive vestibular conditioning. There was faster conditioning of people with vestibular instability.

Hypokinesia: Long-term restriction of motor activity made it possible to describe hypokinesia as a unique factor that leads to alteration of all functional systems of the body. Hypokinesia, which has a prolonged adverse effect on functional capabilities, leads inevitably to a change in system resistance.

This question has not been sufficiently investigated as it relates to the use of radioprotective agents under such conditions. A. V. Sabayev, who studied permeability of the histohematic barriers (HHB) in experiments with hypokinetic animals, concluded that cystamine and mexamine given on the 10th day of hypokinesia increased HHB permeability which had been diminished due to restricted mobility [58]. This enabled him to maintain that the protective effect of protectors under

such conditions must be retained, since passage thereof through biological membranes and accumulation in radiosensitive structures is of some significance to the mechanism of their action. L. Ya. Kolemeyeva et al. [59] demonstrated that there was virtually no change in the radioprotective effect of cystamine and mexamine on mice whose movements were restricted for 5-15 days. Subsequently, with increased duration of hypokinesia up to 60 days, there was 2.2-3.5-fold decrease in radioprotective efficacy of these agents. This phenomenon could be based on hemodynamic disorders, the asthenic syndrome and impaired permeability and, consequently, impaired absorption of the given agents.

Hypoxia, hyperoxia: The antihypoxic effect of gutimin has been studied with the most varied forms of hypoxia [60-66]. M. V. Korablev and P. I. Lukiyenko [65, 67], who conducted experiments on rats and mice, showed that several derivatives of dithiocarbamic acid and thiourea given in the presence of acute hypoxia protected the animals from death to varying degrees. As for other radioprotectors, according to different authors, some attenuate and others enhance animal resistance to hypoxia. For example, according to Bacq et al. [68] and Scott [69], administration of cystamine or cysteamine to rats or mice rendered them less resistant to low barometric pressure and hypoxia. Analogous results were obtained by other authors with respect to these agents and AET [70, 71] in studies of acute hypoxic and hypoxemic hypoxia. At the same time, it was demonstrated elsewhere [13, 14, 72, 73] that cystamine and some of its derivatives enhanced animal resistance to hypoxia, lowering oxygen tension in the brain and body temperature. The antihypoxic effects of cystamine, AET, serotonin and mexamine have also been described in experiments with mice [74]. There has been a report of increased resistance to hypoxia after administration of cystaphos [75].

While there is no agreement among scientists concerning the use of sulfur-containing radioprotectors as antihypoxants, many researchers agree that amine protectors--serotonin or mexamine--enhance animal (including dogs) resistance to acute hypoxia [76-83]. It was noted that the antihypoxic effect of mexamine depends on dosage and time. For example, a maximum survival effect was obtained when mice were given this protector 30 min (15 mg/kg) prior to acute hypoxia (4% oxygen) [84]. Preadaptation to hypoxia improves appreciably the tolerance of subtoxic doses of mexamine by dogs [85]. Mexamine as an antioxidant attenuates changes in activity of oxidative enzymes in the liver, adrenals and myocardium, causing faster recovery of structures under hypoxic conditions [80]. It has been shown that administration of this protector to dogs was associated with a 1.0-1.2°C drop of body temperature [81].

Enhancement of resistance to hypoxia after giving ATP has been reported [86-90]. A more comprehensive study of this phenomenon, which was conducted by P. I. Lukiyenko [91-93], revealed that not only ATP, but AMP, ADP, adenosine and other adenine compounds enhanced animal resistance to acute hypoxia. This author voiced the opinion that macroergic phosphages increase the rate of utilization of oxygen in the brain, while oxygen uptake by muscles does not change.

Some adaptogens--eleuterococcus [75, 94], ginseng [95], vitamin and amino acid complex [96-99]--have been found to enhance resistance to acute hypoxia. It must be noted that ATP, multivitamin complexes and other similar adaptogens are also used as nonspecific protection in the presence of radiation pathology.

According to P. P. Saksonov [100], hypoxia with oxygen level of ≈10%, when this factor is used once prior to or during brief acute irradiation, can already be viewed as a means of radioprotection in aerospace medical practice. Many works have demonstrated enhancement of the radioprotective effect when animals were exposed to radiation in an environment with less than 10% oxygen after being given radioprotectors [84, 101-110]. In this case, the mechanism of radiation protection is apparently not limited to additivity of oxygen effects of both factors, although they do not play the smallest role. Gutimin did not diminish the radioprotective effect of acute hypoxia in epxeriments on mice, rats and dogs [62, 111, 112].

Apparently, the nature of the effect of hypoxia after irradiation depends on the period of radiation damage during which it acts and mode thereof. V. V. Antipov and M. V. Vasin [74], who studied mouse reactivity to acute hypoxic hypoxia on the first postradiation day, demonstrated that animals given radioprotectors were more resistant to it than unprotected ones.

Hyperoxia (elevated oxygen content), like breathing pure oxygen, can aggravate radiation damage [113, 114]. According to the results of early studies, an increase in ambient oxygen pressure at the time of irradiation diminished radioprotective activity of serotonin, but had an insignificant effect on protection with cysteamine, cystamine and AET [115-117]. In more recent studies in this direction, breathing with pure oxygen or elevated level thereof in the atmosphere under normobaric conditions had no modifying effect on the efficacy of certain thiol and amine radioprotectors [114, 118-120]. Most researchers do not consider a brief elevation of ambient oxygen content to be a hindrance to the effective use of radioprotective agents. There are data indicating that the protector, gammaphos, is effective under hyperbaric conditions also [121].

Thus, the above data on the effects of radioprotective agents on reactivity of animals exposed to the stressor effects of a number of factors inherent in space flights demonstrated with examples of accelerations, vibration and hypoxia that radioprotective agents can alter the organism's reactions, both in the direction of attenuation and enhancement of sensitivity to the above-mentioned factors. There are often phasic changes in reactivity (in the case, for example, of accelerations and vibration): decrease in the first hour, restoration and increase thereafter. There can be analogous change in sensitivity to the agents themselves under the influence of prior exposure to dynamic factors. Dosage and nature of the radioprotector, combination thereof with pharmaceutical supplements, as well as species of animals, are very important. Different authors report dissimilar data concerning the same radioprotectors. This also applies to changes in resistance to hypoxia after administration of radioprotective agents. It should be noted that amine protectors usually enhance animal resistance to hypoxia.

All of the studies discussed are characterized by the use of diverse methodological procedures used to assess resistance. Concurrent or successive exposure to radiation and each of the above-mentioned factors can alter appreciably the overall reactivity of the organism. One should never forget that when testing reactivity to a radioprotective agent we are dealing with one or at most two artificially isolated extreme factors, and they do not always simulate completely real ones. During a space flight, however, there is always a set of factors. This complicates significantly experimental evaluation of reactivity of the organism under such conditions to the drugs given, including radioprotective agents. Nevertheless,

analysis of experimental studies of different animal species (mice, rats, rabbits, dogs) indicates that some radioprotectors (cystamine, cysteamine, AET, cystapnos, mexamine) also manifest their specific radioprotective activity when there are combinations of ionizing radiation with rectilinear and radial accelerations (G forces), vibration, motion sickness, brief hypodynamia, acute hypoxia and hyperoxia. The results obtained with adaptogens merit attention: while enhancing radioresistance, they improved resistance to nonradiation flight factors (accelerations, motion, hypoxia). This circumstance acquires special significance with regard to validation of the use of a given radioprotective agent during space flights. At the same time, the inadequate and occasionally distorted effect of drugs in the presence of hypokinesia [27], as well as the demonstrated attenuation of radioprotective activity of some agents at the late stages of hypokinesia [59], make it imperative to conduct more in-depth studies of reactivity of the organism to radioprotective agents under the unusual conditions of prolonged restriction of motor activity.

The mechanisms of effects of nonradiation flight factors modified by protectors are complex and diverse. They have not been sufficiently investigated by far. Efforts to attribute their action to antagonistic or synergistic effects on the cardiovascular, nervous and endocrine systems, metabolic processes (primarily tissular oxygen tension) and permeability of histohematic barriers are of definite significance. The very closest attention must be given to investigation of this question.

On the basis of the foregoing, it can be stated that it is possible to use drugs to enhance radioresistance during flights; however, one should proceed with some caution in recommending a specific inflight radioprotective agent. The results of studies with the participation of man have confirmed the assumption that intake of the short-acting radioprotector ambratin and prolonged-action protector amitetravit has no adverse effect on the human body according to tests with endurance of motion and prolonged accelerations. For this reason, they have been recommended as radioprotective agents for use during manned flights aboard the Soyuz series of spacecraft [46, 122].

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SOLAR ACTIVITY, DYNAMICS OF OZONOSPHERE AND POSSIBLE ROLE OF ULTRAVIOLET RADIATION IN HELIOBIOLOGY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 81 (manuscript received 19 Feb 81) pp 12-15

[Article by B. M. Vladimirskiy]

[English abstract from source] Solar activity influences the ozonosphere thickness, thus changing the intensity of the near-earth ultraviolet radiation in the B band. In certain regions the radiation may change by 10-15%, with solar activity varying from its maximum to minimum. The variations in the ultraviolet intensity are very likely to be environmentally important. Thus, solar ultraviolet radiation at λ = 290-340 nm acts as one more physical agent transferring the effect of solar activity into the biosphere.

[Text] Solar activity affects the thickness of the ozonosphere. This is associated with change in intensity of near-earth UV [ultraviolet] radiation in the B band. In some regions, there can be 10-15% changes in intensity of maximum to minimum solar activity. These variations are probably ecologically significant. Thus, solar UV radiation (wavelength 290-340 nm) is another physical agent that transfers the effects of solar activity to the biosphere.

The problem of effects of variations in solar activity on the biosphere has gained some theoretical validation in recent years. The main working hypothesis, that could serve as the basis of an explanation for the presence of such an influence is that organisms (or ecosystems) react to amplitude and spectrum changes in background electromagnetic fields in the ranges of low and extra low frequencies, which are closely related to solar activity [1]. Data indicative of the high sensitivity of many organisms to weak extra-low-frequency electromagnetic fields, which were obtained in laboratory experiments [2-4], speak in favor of this hypothesis. It becomes possible to comprehend many effects of solar activity in the biosphere, including those previously demonstrated in medical statistics [5], within the framework of this hypothesis.

However, there are some facts and observations that do not conform to the scheme, in which perturbations of the electromagnetic field are the active agent. Statistics on incidence of skin cancer in man can serve as a concrete example. These data, which were analyzed for the USSR [6], United States [7] and Canada [8], demonstrate a distinct 11-year cycle. In view of the relevant data on etiology of these diseases and their geographic distribution, as well as the phase correlation between the morbidity curve and curve of indexes of solar activity (which changes

with the latitude), it is difficult to explain the 11-year cycle. Nor do other possible channels of transmission of solar activity into the biosphere discussed in the literature offer clarification, for example, infrasonic noise [9] or minor changes in atmospheric radioactivity related to magnetic perturbation [10]. It is a known fact that one of the causes of malignant melanoma is exposure of the skin to the UV component of solar radiation. Proceeding from this, the simplest explanation for appearance of 11-year cycles in the above-mentioned statistics would be that there are corresponding cyclic variations in the flux of near-earth UV radiation. We submit below some data and considerations, which show that such variations of adequate amplitude do indeed occur. The distinctions of these variations are such, that they enable us to comprehend the main patterns of distribution and change in incidence of skin cancer. These variations could have other consequences also, and apparently we must concede that there is one more physical agent by means of which variations of solar activity can affect biological phenomena. It must be noted that the very thought that fluctuations in the flux of UV radiation may have a role in heliobiological effects is by no means new. It was expounded in a general form by Douglass as far back as 1927 [11], and subsequently discussed by other authors [7, 12].

As we know, earth's atmosphere, which forms solar UV radiation close to 290 nm, lets through a narrow spectral band that overlaps the edge of the band of DNA and protein absorption, which explains the high biological effectiveness of radiation in the wavelength range of 280-340 nm. In this range, solar radiation beyond the atmosphere is virtually unrelated to the level of solar activity. Variations of radiation at the bottom of the atmosphere in this range occur because of changes in thickness of the ozone layer that shield's earth's surface. In the center of the main band of ozone absorption (260 nm, Hartly's band), absorption is so great that changes in thickness of the ozonosphere over a wide range have absolutely no effect on the intensity of near-earth radiation. However, on the edge of the band close to the maximum effectiveness of carcinogenic effect on the skin--290-300 nm [13]--relatively minor changes in the ozonosphere lead to appreciable changes in the flux of radiation on earth's surface. Estimates made in recent years, in connection with discussion of the anthropogenic effect on the ozonosphere are as follows: when there is a 1% decrease in thickness of the ozonosphere at moderate latitudes the intensity of radiation in the B band (280-340 nm) increases by about 2%, which should lead to about 4% increase in incidence of skin cancer [14, 15] (of course, these estimates are rather approximate).

The thickness of the ozone layer at a given point is determined by interaction of many processes, such as change in short-wave solar radiation (260 nm), occurrence of many aeronomic reactions, atmospheric circulation. For a long time, the question of relationship between ozone concentration and solar activity was the subject of debates. At the present time, there has been experimental determination of some effects of solar activity in the ozonosphere. For example, according to satellite readings [16], the global ozone content on the short time scale shows a distinct correlation with solar activity (r = +0.75). Data have been published [17, 18] to the effect that the average (for example, for the northern hemisphere) change in overall ozone content from maximum to minimum solar activity does not exceed 1%. The figure may be considerably higher for individually considered stations. For example, at the Arosa Station (Switzerland, 47° north latitude), the overall maximum-minimum variation was about 8% in 1935-1975. At temperate latitudes, the maximum concentration of ozone is usually observed 3 years after

maximum solar activity. It must be noted that this lag diminishes with increase in latitude. This conforms well with data to the effect that maximum incidence of malignant melanoma [7, 8] at high latitudes coincides with maximum solar activity, whereas at low latitudes it either coincides with the maximum or is about 2 years "behind" maximum activity. The amplitude of changes in thickness of the ozonosphere from maximum to minimum activity (if we do not use the global average) is quite adequate for explaining the 11-year cycle in the cited data [6-8], if we consider the above estimates to be correct.

Unlike electromagnetic perturbations, which transmit the effects of solar activity into the biosphere "instantaneously" (hours, days), the variations of UV radiation under discussion are essential to comprehension of heliobiological phenomena on a time scale of the order of several years, since in this case a certain dose must accumulate. Moreover, the effects attributable to appearance of an additional flux of UV radiation should not be global. This is related to the dependence of the radiation flux on zenithal distance of the sun, decrease in thickness of the ozonosphere toward the equator, as well as presence of clouds. In geographic regions where cloudy days are more likely between August and October (northern hemisphere), when there is the seasonal minimum of total ozone concentration, the additional flux of radiation could be very minimal. Since tropospheric circulation is a complex function of solar activity, there may be regions where the heliobiological effects caused by variations in ozonosphere thickness may not be noticed.

At the present time, we cannot trace the most important consequences of UV radiation because the ecological role of such radiation (290-340 nm) has been little-studied, as well as due to the complexity of ecosystems. We can only list some of the areas, in which the effects under discussion could be theoretically important.

It was recently discovered that the dose of solar UV radiation in the B band to which organisms inhabiting the superficial layers of water (salt and fresh water phytoplankton and zooplankton) are naturally exposed is very close to the tolerance dose for these organisms [19]. If this is so, the parameters of the corresponding biocenoses (including productivity) should be modulated by the 11-year cycle of solar activity. Perhaps this is also related to the existence of an 11-year cycle in data pertaining to catching certain commercial fish.

As we know, changes in intensity of UV radiation could affect the intensity of photosynthesis. An increase in intensity of radiation to which high-altitude flora is exposed could lead to appreciable depression of vital functions, since in this case the amplitude of increase in intensity is relativley high. In this regard, it is perhaps no coincidence that the minimum of timber increment in mountain regions of Eurasia occurs in the second year [22] after maximum solar activity (like the increase in cases of malignant melanoma at temperate latitudes) [7]. Incidentally, on the northern edges of forests, the increase in trees varies over an 11-year cycle, in phase with solar activity [22]. It is also well-known that exposure of plant organisms to an additional flux of UV radiation leads to an increase in levels of biologically active substances, for example, vitamins [20]. If the increase in vitamin E content of plants in a given region is indeed one of the essential factors regulating the size of small rodent populations [21], we cannot rule out the possibility that synchronization of the rhythm of changes in number of these animals with solar activity occurs expressly via the dynamics of the ozonosphere.

Of course, fluctuations in intensity of UV radiation must lead to some changes in the composition of bacterial flora of the air and superficial layer of water basins. If the changes in number of mutations in time [23] are attributable to the exogenous effect of some ecological factor, probably variations of UV radiation could be such a factor. The process may take place in many steps. Mutants, appearance of which can be partially determined on the basis of outbreaks of infectious diseases, should in such a case appear during periods of minimal overall concentration of ozone, mainly at low latitudes, in late summer and fall (for the northern hemisphere). The capacity of UV radiation to restore inactivated viruses within cells should also lead to the same effects.

This brief discussion leads us to formulate the following conclusion: changes in intensity of near-earth UV radiation in the B band due to dynamics of the ozonosphere are probably of ecological significance. This component of radiation is perhaps one more physical agent that transfers the effect of solar activity into the biosphere.

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

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STRESS AND BIOLOGICAL RHYTHMS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 27 Apr 81) pp 16-20

[Article by S. I. Stepanova]

[English abstract from source] Numerous data give evidence that the reactions of the human body to diverse stimuli vary in an oscillatory, wave-like pattern. This phenomenon is associated with a general biological law of the wave-like pattern of adaptive processes, according to which they are realized at any stage (anxiety, resistance, depletion) in an oscillatory pattern. The wave-like pattern of the adaptive process is an expression of the dialectic law of unity and struggle of opposites; in this case, unity and struggle of construction and destruction, maintaining continuous self-reproduction and self-preservation of a living system in its environment. In order to improve the methods and procedures for sustaining man-in-space, further studies are required to investigate specific manifestations of this law.

[Text] The thesis that rhythm is a universal property of living systems is one of the principal ones in modern biology. When one says that all vital functions are rhythmic, one usually refers to a healthy organism functioning under normal conditions without any perturbing factors. However, as shown by numerous facts, the organism's reactions to the most diverse stimulation also occur in an oscillatory, undulatory fashion. This undulation constitutes the initial periodicity that has been transformed in a specific way. If we consider life as a continuous process of adaptation, viewed as the capacity for self-preservation, self-support of the organism, there is every reason to refer to the general biological law of undulatory nature of the adaptation process, whose essence consists of the fact that this process occurs in an oscillatory mode in any of its phases (anxiety, resistance, depletion).

Recognition of the fact that phenomena of life and adaptation are one and the same inevitably ensues from the basic thesis of biology of the unity of the organism and environment. As far back as 1867, Claude Bernard said: "...if we disturb or destroy an organism without touching its environment, life will cease immediately; the same will happen if we alter or destroy the environment, without touching the organism. Thus, a phenomenon of life is not contained in either the organism or environment separately, it is, so to speak, the result of contact between the

organism and the environment that surrounds it" [1]. But expressly this result, which is a continuous process of equilibrating the organism with the environment, was named adaptation. It is based on two opposite phenomena--breakdown and synthesis of chemical compounds in the organisms. The capacity for breakdown, and rapid breakdown at that, is just as necessary for self-support of the organism as the capacity for rapid synthesis, restoration. The unity of these two processes--breakdown and synthesis--enables the organism to withstand the devastating, deleterious effects of the environment (and, incidentally, to utilize its positive aspects). "The organism is stable," Richet maintained, " since it is modifiable" (cited in [2], p 1?) and, further, "... if I were to try to formulate this self-protection of the organism, which constitutes the entire content of physiology in our opinion, I would say: a living being ... perpetually renews itself and perpetually remains unchanged" ([3], p 97). To provide constancy on the basis of variability, constancy by means of inconstancy--such is the dialectical formula of life, formula of adaptation. Destruction (dissimilation, catabolism) is in essence just as active a self-preservation tool of the living organism as creation (assimilation, anabolism). Breakdown and synthesis are to inseparably linked elements of the same process of exchange of substances [metabolism] between the environment and organism, which provides for continuous self-reproduction of the latter

Apparently, the organism, which is subject to constant destruction and renewal, can exist for a long time and in a stable manner only if there is a balance between these two mutually exclusive processes. From the dialectical point of view, this balance is not static, immobile; on the contrary, it implies continuous opposition between destruction and creation, in the course of which one or the other of these two factors alternately has the advantage, i.e., one observes a periodic change of leadership of both sides in the forefront of the adaptation process. As long as this periodicity is retained the organism exists; but as soon as either side prevails in the struggle between destruction and creation the organism perishes and, at the same time, the process of individual adaptation is terminated.

As we have noted above, adaptation is a continuous process that never stops for an instant in a living organism. Selye, who used the term "stress" to designate the adaptation phenomenon (more precisely, the aggregate of its nonspecific manifestations), wrote: "Regardless of what you do or what happens to you, there is always a need for energy to maintain life, resist attack and adjust to constantly changing exogenous factors. Even in a state of total relaxation, sleeping man experiences some stress. The heart continues to pump blood, the intestine continues to digest yesterday's supper, while the respiratory muscles provide for movement of the chest. Even the brain does not rest completely during periods of dreams.... Total freedom from stress means death" ([4], p 30).*

The balance between the organism and environment is being constantly disrupted, not only by virtue of variability, instability of the environment, but because

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*It is expressly because stress is a constant companion of life, its inalienable attribute, that it is expedient to make a distinction between resting [peaceful] stress (i.e., stress that does not exceed the ordinary, everyday level) and stress caused by stimuli that are extraordinary in force and nature. Hereafter, when discussing stress, we shall be referring to the latter case, the result of factors that are unusual in force and nature.

of the extreme dynamism of the organism itself in the course if its individual development, from the moment of conception to the moment of death. F. Engels said: "... life consists primarily of expressly the fact that a living being is the same and yet different at each point in time" ([5], p 120). For this reason, if we were to imagine, purely abstractly, that the organism finds itself in a dead, static, unchanged environment, it would still be compelled, even under such conditions, to adapt to it at every moment, since its own variability would prevent achieving stable equilibrium with this environment.

We have discussed two extremely important properties of the adaptation phenomenon, continuity of processes from the moment of conception to the moment of death and periodicity of processes upon which it is based. When we refer to periodicity of vital processes, it should be borne in mind that the terms "periodicity," or "rhythm" signify, strictly speaking, many repetitions of the same event or production of the same state at equal intervals. However, this never actually occurs in nature. N. Ya. Perna [6] stated that any periodic process is a progressive process, and for this reason each successive period is not a total repetition of preceding ones; rather, it is superimposed over these preceding periods as a new step. In other words, a real physical rhythm (in animate or inanimate nature) is always a "repetition without repetition" (in the expression of N. A. Bernshteyn). In a living organism, the cycles that follow one another differ in parameters--duration of period, amplitude, level. When the adaptation process occurs calmly, without particular shock to the organism, when the stimuli affecting the organism do not exceed the ordinary everyday level, the range of these differences is narrow, and we are justified in using the concepts of "rhythm" or "periodicity" to describe the fluctuating processes in the living system. If, however, the adaptation process is intensive ["violent"], associated with marked and rapidly developing changes in the organism, which may be due to the effects of powerful stimuli or the special dynamism of the organism at certain stages of individual development (embryonic stage, postnatal ontogenesis, puberty), the state of the organism changes very noticeably from cycle to cycle, and the oscillatory processes lose, to some extent or other, their regularity and uniformity.

A distortion of biological rhythm and transformation thereof to aperiodic fluctuations are indicative of drastic exacerbation of internal contradictions in the adaptation process. The changes in initial periodicity under stress may also be manifested by an increase in amplitude of the oscillatory process due to activation of expenditure and replenishment of energetic and plastic resources of the organism, i.e., activation of both aspects of metabolism--catabolism and anabolism. The reaction to a potent agent consists of rapid mobilization, activation of concerned processes, while a high degree of activation is the prerequisite for intensive depletion, destruction and inevitable decrease in activity. In other words, high activity leads to severe depletion and requires restoration. But, on the other hand, intensive restoration [recovery], which is associated with active accumulation of functional reserves, requires expenditure of these reserves. Such is the mechanism of increase in amplitude of initial oscillations under stress. H. Spencer [7, (p 417)] wrote: "The greater than usual transformation of molecular motion into visible motion is soon followed by a more than usual intake of food, which serves as the source of molecular motion, and after a long period of expending the spare capital of the system there is a desire for a long rest, during which the spare capital is replenished." We see that, here, H. Spencer mentions another factor, in addition to the increase in amplitude, namely, increase in duration of the rhythm

period under stress, leading to increased efficiency of recovery processes and postponement of the moment of maximum tension [8, 9]. Finally, another important effect of stress is spatial synchronization of rhythms of different functional structures, both intraorganic and interorganic. According to the law of alternating activity of functional structures (G. N. Kryzhanovskiy, cited in [10]), in a state of relative rest the organism functions in parts, each of which consists of a group of cells with the same rhythm of work and rest. The rhythms of the different functioning parts are not synchronized with one another. Continuous function of a whole organ, without straining it, is based on alternate function of cellular structures. However, with stress factors one may observe mutual synchronization of rhythms of different functional structures, which provides for mobilization of all reserves, as a result of which the system functions in a particularly intensive rhythm. Such mutual synchronization must, apparently, be associated with an increase in rhythm amplitude and, perhaps, increase in duration of its period as a result of simultaneous involvement in activity of many functional units that are heterogeneous in their inertia.

Thus, an increase in amplitude of rhythmic processes involved in the stress reaction and lower frequency of their oscillations are the biorhythmological indicators of a high degree of stress. Schematically, the reaction to a single acute stimulus can be conceived as an initial increase in amplitude and period of initial rhythm, with gradual extinction of amplitude of oscillations, decrease in their period and final restoration of initial periodicity. This is illustrated in Figure 1. It must be stressed that this is merely a rather general scheme characterizing the course of a reaction to a single acute stimulus. In the first place, it illustrates the oscillatory nature of the process at the resistance stage (before the stimulus and after restoration of initial rhythm) and anxiety [alarm] (the three large waves in the middle); in the second place, it shows the increase in amplitude and period of the rhythm at the anxiety stage and, in the third place, the gradual extinction of oscillations and return to their original appearance. It is hardly necessary to mention that in a real situation there are not necessarily three waves at the stage of anxiety. This scheme does not describe the direction of the initial deviation (i.e., the one observed immediately after the stimulus) of parameters from their initial values; it merely notes the fact that such deviation occurs. The location of the peak of the first wave, which is referable to the anxiety stage, above the midline on the tracing does not signify that the reaction always begins with an upward motion (i.e., increase in numerical value of the recorded parameter); it may move down also. Finally, the scheme illustrated in Figure 1 does not take into consideration the complexity of the oscillatory process, its integral nature. It illustrates the dynamics of a stress reaction in the sphere of an elementary, solitary vital process, whereas the parameters of vital function of an organism that are really recorded always bear the mark of several processes. Perhaps, expressly this flaw of the scheme explains the fact that in reality the extinction of oscillations after delivery of a single stress agent may not coincide with this scheme in that we would observe a decrease instead of gradual increase in frequency of oscillation. Let us imagine a certain oscillatory process formed of three components: high-frequency, low-frequency and intermediate (Figure 2). Right after delivery of the stimulus, the recorded reaction will be determined primarily by the state of the high-frequency component, since it will present the most demonstrative changes being the least inert component. But, by virtue of its minimal inertness, it also reverts to normal faster and then, oscillations of a lower frequency will move to the fore, etc. As a result, we shall observe gradual increase in oscillation period as the stress reaction regresses.

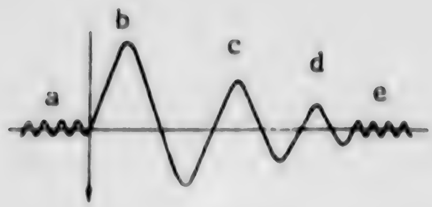

Figure 1.
Undulatory dynamics of arbitrary elementary functional parameter at different phases of adaptation process
a, e) resistance stages
b, c, d) anxiety stages
Arrow shows time of delivery of solitary stimulus

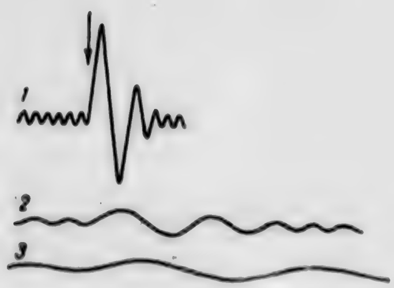

Figure 2.
High-frequency (1), intermediate (2) and low-frequency (3) components of single oscillatory process (shown separately) before and after solitary stimulus. Arrow shows time of stimulation

Moreover, the different special biological oscillations are always governed by the demands of the integral organism, and this could cause other deviations from the submitted scheme (for example, an increase in base frequency of oscillations at the anxiety stage instead of a decrease).

As for the reaction to a prolonged stress agent, it is extremely difficult to render it in the form of a single, even approximate, scheme. However, in this case there is no question but that the reaction is always undulatory. Apparently, the immediate response to an acute and chronic factor must be stereotypical, because the effect of the first encounter with a stimulus is not related to its duration, short- or long-term. Consequently, at the very start of chronic stimulation, as in the first phase of the reaction to an acute stimulus, we can observe an increase in amplitude and period of initial oscillations. Subsequently, when stimulation is continued, the amplitude and period of oscillations may change in the direction of both increase and decrease; the level near which these oscillations occur may drop below or, on the contrary, rise above the base level. However, the oscillations never disappear. They pervade all three stages of the adaptation process: anxiety, resistance and depletion. Each of these stages is characterized by undulatory reactions.

In summary, it should be stressed once more that adaptation is an oscillatory, undulatory process and that adaptation reactions (both specific and nonspecific) occur in an oscillatory mode. This waviness is a general biological pattern and it reflects the struggle between two mutually exclusive elements of the adaptation (vital) process--destruction and creation, catabolism and anabolism. Consideration of the law of undulatory nature of the adaptation process in space opens the way for reliable forecasting of the dynamics of general state and different functions of cosmonauts during flights. It is imperative to make a special study of this phenomenon in order to further refine the set of measures related to the support of man's life in space.

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RESULTS OF STUDIES OF COSMONAUTS' VESTIBULAR FUNCTION AND SPATIAL PERCEPTION

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[Article by I. Ya. Yakovleva, L. N. Kornilova, I. K. Tarasov and V. N. Alekseyev]

[English abstract from source] The results of studying the vestibular function and the function of spatial perception in 26 cosmonauts before and after 30 space flights are discussed. The typical postflight changes in these functions were: an increase in the reactivity of the otolith organ, a decrease in the sensitivity of semicircular canals, a decline in the accuracy of perception of spatial coordinates, asymmetry of most parameters, development of illusionary reactions inflight. The cosmonauts also showed individual variations with respect to the degree of the above responses, the dynamics and length of adaptation, the development of the motion sickness symptom-complex, etc. At R+0 some cosmonauts exhibited a change in the direction of the eye counter-rotation, i.e., the negative otolith reflex or at turn towards the tilt direction. Possible mechanisms of these vestibular changes are discussed.

[Text] Many cosmonauts develop disturbances in flight referable to spatial perception and symptoms of motion sickness.

These disorders are the most marked at the time of initial adaptation to weightlessness and first stage of the period of readaptation to conditions on earth.

Many opinions and hypotheses have been expounded concerning the genesis of the symptoms of motion sickness and illusions of spatial position during space flights. However, most researchers attribute the chief significance to unusual function of the vestibular system and systems that interact with it in weightlessness [1-14].

No doubt, studies of sensory systems during actual space flights are of greatest importance to learning the neurophysiological mechanisms of development of motion sickness in weightlessness. At the same time, ground-based studies conducted before and after flights make it possible to expound a hypothesis about the possible mechanisms of changes observed in flight.

Our objective here was to investigate the phenomenology of vestibular system reactions and spatial perception in weightlessness on the basis of preflight and postflight examination of cosmonauts.

Methods

We examined 24 cosmona s who had made flights in craft of the Soyuz type and the Soyuz-Salyut orbital c plex, 6 of whom had participated in 2 missions. These studies were made with respect to 10 short-term (4 and 7 days) and 5 long-term missions (30, 96, 140 and 175 days).

All of the cosmonauts underwent an expert clinical and physiological examination and were deemed healthy, and this also applied to the condition of the ear, nose and throat.

Otolith function was evaluated by the magnitude of circumduction ["counterrotation"] reaction of the eyeball when moving from vertical position to the right and left side in horizontal position. We used a modification of the Fischer and Fluur method of indirect otolithometry [15, 16].

The function of the semicircular canals was evaluated by testing threshold sensitivity to an adequate stimulus (according to nystagmus and sensory component).

We examined the distinctions of interaction between the otolith system and semicircular canals according to nystagmus and sensory component by means of the modified "otolith reaction" (OR) test of V. I. Voyachek (graded angular accelerations repeated after 2-5 min, followed by change in position graded in speed and direction). The intensity of autonomic reactions (AR) was evaluated by the classification of K. L. Khilov and data from tracings of pulse rate (PR), respiration (RR), arterial pressure (AP) and electrocardiogram (EKG).

Perception of spatial coordinates was tested with a portable "Vertical" instrument with the subjects in seated position, in horizontal position on the right and left side.

A special questionnaire was used to assess reactions during space flights according to the subject accounts of the cosmonauts.

The otolith reflex, thresholds of angular accelerations and spatial perception were tested 3 to 6 times in the background period (30-45 days before the flights) and the same number of times on 0 day or 1st-2d, 4th-5th days, and on the 8th-9th days of long missions, as well as 14th day in some cases or 1 month after them.

We determined the standards for all tested parameters on the basis of prior testing of 112 healthy men 25-40 years of age.

The normal magnitude of the otolithic reflex constituted $12\pm7°$ ($3°$ asymmetry), error of perception of spatial coordinates in vertical position constituted $0.67\pm0.3°$ and on the side $18\pm5°$ ($5°$ asymmetry); the thresholds of the semicircular canals constituted $4\pm2°/s^2$ for nystagmus and $3\pm2°/s^2$ for illusion (in both cases $2°/s^2$ asymmetry); nystagmus and illusions with exposure to angular accelerations lasted 31 ± 9 and 14 ± 6 s, respectively, when the position was not changed, 22 ± 5 and 9 ± 3 s with change in position.

Results and Discussion

Preflight tests: All but three cosmonauts presented otolithic reflexes that were in the range of fluctuations of the physiological norm. The reflex was symmetrical, or else the asymmetry did not exceed physiological scatter. In both tests, the reflex parameters were low (1-2°) for the commanders (CDR) of Soyuz-22 and Soyuz-31. Asymmetry of the reflex exceeded the physiological scatter, constituting 8 and 9° for the CDR of Soyuz-26 and flight engineer (FLE) of Soyuz 32, respectively.

All of the comsonauts, with the exception of the CDR of the first mission aboard the Soyuz-Salyut-6 orbital complex, presented threshold sensitivity of semicircular canals within the range of physiological fluctuations, constituting 2-6°/s^2. The CDR of this mission presented an elevated threshold of sensitivity of semicircular canals, which constituted 11°/s^2, and asymmetry constituted 6°.

There was reciprocal interaction between the semicircular canals and otolith system in 63.4% of the cases: attenuation of semicircular canal reflexes in response to graded change in position. The reflex did not change in 20% of the cases and in 16.6% graded change in position after angular accelerations enhanced the reflexes from the semicircular canals.

Error in perception of spatial coordinates was in the range of physiological fluctuations in the background tests on all of the cosmonauts (except three).

There was asymmetrical perception of spatial coordinates due to a substantial (up to 32-38°) increase in error when lying on the left side in the FLE of Soyuz-22, Soyuz-T-2 and first mission aboard the Soyuz-Salyut-6 orbital complex, as well as CDR of Soyuz-28.

Thus, in the preflight period the tested characteristics of vestibular function were in the range of the physiological norm in most cosmonauts. At the same time, 10 of them presented individual distinctions of some parameters. Three cosmonauts, who presented a diminished otolithic reflex and asymmetric accuracy of perception of spatial coordinates in the background period, tolerated the missions well without any marked symptoms of motion sickness. Seven cosmonauts, on whom we recorded heightened threshold sensitivity of semicircular canals in the background period, as well as accentuation of somatosensory reflexes of the semicircular canals upon graded stimulation of the otolithic system and asymmetry of the otolithic reflex, developed the symptom-complex of seasickness during flights.

Results of interrogating cosmonauts: Interrogation of the cosmonauts on the 1st day after space missions revealed that illusory reactions occurred more often in flight than autonomic ones. Thus, all but three (CDR and FLE of Soyuz-22, FLE of the third mission aboard the Soyuz-Salyut-6 orbital complex) cosmonauts reported illusory reactions of the inversion type ("hanging upside down"), occasionally in the form of displacement of surrounding objects. In most cases, these reactions occurred immediately after weightlessness began, and in some cosmonauts 2 h later. The initially occurring illusion lasted a few minutes in some cosmonauts and 4 or more hours in others. The illusion recurred sporadically during the flight, most often at times of increased motor activity or under the influence of optokinetic stimuli. Some cosmonauts were able to suppress illusions by means of fixing their eyes on some object, immobilizing themselves in the seat, as well as autotraining (relaxation exercises).

Vestibulovegetative discomfort in the form of vertigo, nausea, heaviness of the stomach and, occasionally, vomiting, was noted in 15 of 30 cosmonauts surveyed. The reactions varied in severity and duration (from a few hours to 3-7 days). They also appeared at different times (1 h after onset of weightlessness, or else after 1-1.5 days). According to the reports of 10 cosmonauts, these signs increased in severity during motor activity and in 3 cases under the influence of optokinetic stimulation. Four cosmonauts reported a definite correlation between development of vestibulovegetative disturbances and sensation of "blood rushing" to the head.

Various symptoms of blood rushing to the head were noted in all subjects (heaviness of the head, congested nose, puffy face, etc.); however, most cosmonauts did not observe that these signs affected development of vestibular discomfort.

We can arbitrarily distinguish between three types of adaptation to flight factors: resistance--absence of autonomic and sensory discomfort, or mild illusory reactions (9 people); violent--very marked reactions lasting for a relatively short (2-3 days) time (8 people); torpid (protracted)--mild symptoms of vestibulovegetative discomfort and sensory disturbances (7 people). In 2 cosmonauts of this group who participated in 7-day missions, according to subjective evaluation there was never complete adaptation to space flight conditions.

Results of postflight studies: After the flights, 6 out of 24 cosmonauts tested on 0-1st days presented sensory reactions (vertigo upon turning the head and changing position, in 2 cases the illusion of bending down 10-15° in horizontal position) and varying degrees of vestibulovegetative disturbances (heavy sensation in the stomach, nausea, in 2 cases vomiting). Virtually all of the cosmonauts presented statokinetic disorders at this time, in the form of shaky gait and lack of stability in Romberg's position.

Our findings indicate that there are some tendencies of change in the otolithic reflex, threshold sensitivity of semicircular canals, perception of spatial coordinates, nature of interaction between the otolith system and semicircular canals.

We observed changes in otolith function on the 1st-2d day after both long-term flights (in all of the cosmonauts we tested) and after short-term missions (in 14 out of 18 subjects). In 16 cases, we demonstrated hyperreflexia (bilateral or unilateral) of the otolithic reflex (21-38° versus the norm of 12±7°). Relative hyporeflexia was found in 2 cosmonauts (after 175 days of flight in 1 of them and after 7 days of flight in the other) on the 1st day: decline of reflex from 12 to 5° in the former and from 15 to 6° in the latter.

Another distinction of change in the otolithic reflex was appearance of asymmetry reaching 8-14° (normally up to 3°). Reflex asymmetry was more marked (14°) and observed in all subjects participating in long-term missions, as well as in 4 out of 18 cases after short-term flights. We observed a change in postflight direction of asymmetry in 5 of the tested cosmonauts. A tendency toward normalization of the demonstrated changes was observed on the 2d-4th days after short-term flights, 8th-9th days after long-term ones and in 2 cosmonauts 1 month after the mission.

We should discuss in particular the results of tests performed on 8 cosmonauts on 0 day following short-term missions. Four of them presented no changes, while the other four revealed an unusual reaction to bending in the frontal plane: rotation of eyeballs in the direction of bending. This reaction was recorded in 3-5 tests.

We designated as a negative reflex the change we observed in these cases in direction of the otolith reflex. Examination on the 2d postflight day revealed a positive otolithic reflex (rotation of the eyes in the opposite direction from bending) in three cosmonauts; however, its parameters did not always reach the background level and it remained negative in one case.

The thresholds of the semicircular canals were elevated (10-15°/s^2, versus the norm of 2-6°/s^2) in 8 cosmonauts after long-term flights and 8 after short-term ones. The threshold declined in one cosmonaut after a short-term mission, i.e., elevation of sensitivity of semicircular canals; the thresholds did not change in 13 men. In 4 subjects after long-term missions and 6 after short ones, we observed asymmetric sensitivity (up to 8°/s^2 versus norm of 2°/s^2).

We observed a tendency toward restoration of thresholds on the 4th-5th day after short-term flights, on the 8th-9th day after long-term missions and on the 32d day in 2 cosmonauts. Examination of the effect of bending the body in the sagittal plane on semicircular canal reflexes revealed changes in only 3 cosmonauts, as compared to background levels, following long-term missions.

Perception of spatial coordinates was impaired in all cosmonauts following long-term missions. These changes consisted of either an increase in error to 38° in lateral position (normal 18±5°) and to 3-4° in vertical position (norm is 0±1°), or development of asymmetry, the degree of which reached 14° in lateral positions (normal up to 5°). A tendency toward recovery was observed on the 8th-9th days and in 2 cases on the 32d day.

Analogous changes in spatial perception were observed in 10 out of 20 cosmonauts following short-term flights. Errors in lateral positions also constituted 38° in some cases and 3° when sitting down. A tendency toward recovery was observed on the 2d-4th day.

The changes in the parameters tested were more marked and persisted for a longer time in the postflight period following missions lasting 30, 96 and 140 days than after the 175-day flight. Apparently, this is attributable to a better system of prevention used in this flight, as well as individual flexibility of the cosmonauts' nervous system.

We made a comparative analysis of the data obtained from testing six cosmonauts who participated in two missions. Three of them were tested on the complete program, whereas in the three others we did not test the otolithic reflex in the first mission. Subjectively, all of the cosmonauts reported easier and faster adaptation to flight factors in the second mission. There were five illusory reactions after the first flight and one cosmonaut had such a reaction after the second one; autonomic discomfort was reported by two cosmonauts after the first flight and one after the second.

There were objective signs of impaired otolith function in two out of three subjects after the first flight and in four out of six after the second one.

Thresholds of sensitivity of semicircular canals and their interaction with the otolith system were unchanged after both missions.

Spatial perception was impaired in all of the cosmonauts after the first flight and in four out of six after the second one.

A comparison of flight endurance according to signs of development of motion sickness and of data obtained from background testing of vestibular function and spatial perception revealed that development of motion sickness was observed in the presence of both normal background parameters (in 8 out of 20) and when the tested parameters presented some distinctions (7 out of 10). The following background features were prognostically unfavorable with regard to processes of adaptation to weightlessness: heightened threshold sensitivity of semicircular canals, other than standard interaction of semicircular canals with the otolith system and asymmetry of the otolithic reflex. The presence of functional distinctions of the vestibular system and spatial perception in the background tests was more often associated with development of inflight motion sickness.

However, the rather large number of cases of development of inflight motion sickness among subjects with normal parameters of vestibular function in the background period indicates that not only the initial state of this function, but other factors play a substantial role in onset of vestibulovegetative disorders in the cosmonauts during flights.

A comparison of endurance of the flights to data obtained in postflight tests revealed that changes in the otolith reflex were present in all cosmonauts examined after long-term missions. After short-term flights, the otolith reflex was unchanged in only four cosmonauts, and they had not experienced symptoms of motion sickness during the flight. Asymmetry was observed in all cosmonauts after long-term flights and in four after short-term ones.

Changes in thresholds of semicircular canals (elevation and asymmetry) were also found in virtually all cosmonauts following long-term flights, regardless of endurance of the flight. Postflight findings were in the normal range in only two men who endured the flight differently. Changes in threshold sensitivity of semicircular canals following short-term expeditions, with development of motion sickness, in six cosmonauts, and these parameters were in the normal range in three. Among those who endured short-term missions well, eight presented parameters in the normal range and three had altered parameters.

Changes in the system of spatial perception were demonstrated in all subjects after long-term flights, regardless of endurance. After short-term flights, the tested parameters remained unchanged in seven subjects who tolerated the flight well and in three who developed inflight motion sickness. Changes were noted in four cosmonauts with good tolerance and in six who presented the symptoms of seasickness. Asymmetry was observed in all cosmonauts after long-term missions and in seven after short-term ones.

Analysis of our findings revealed that space flight factors elicited changes in vestibular function and spatial perception. More significant and prolonged changes were observed during longer missions. The demonstrated disturbances had a tendency to recover.

We can refer, to some extent, to changes of a general nature and individual reactions.

The increase in reactivity of the otolith organ, asymmetry of vestibular function, worsening of accuracy of perception of spatial coordinates, diminished threshold sensitivity of the semicircular canals and development of illusions in flight should be classified as general changes; individual reactions include the severity of the above changes, differences in dynamics and term of the readaptation period, development of vestibulovegetative symptoms at the early stage of adaptation to weightlessness and readaptation to ground-based conditions, change in nature of interaction between the otolith system and semicircular canals.

The more frequent changes in the otolith reflex noted after the flights are probably attributable to the specific effect of weightlessness, and apparently they could be one of the consequences of mismatch in sensory system function, impairment of corrective function of the cerebellum and central vestibular structures.

Increased reactivity of the otolith system, which was observed in most cosmonauts after the flights, could be interpreted as the result of a reaction to a powerful stimulus in the form of earth's gravity following the period of "shortage of stimulation" in weightlessness. For some subjects, this stimulus was so strong after returning to earth that it depressed the reflex (on the order of supraliminal inhibition) or altered its direction. We cannot rule out the possibility that the negative reflex observed on 0 day was attributable to phasic changes in neuronal structures responsible for this reflex. Such a distortion of tonic reflexes of ocular muscles had been previously found by Sentagotai during long-term stimulation of the vestibular receptor [7]. In the special studies pursued in the clinic of Prof V. T. Pal'chun, a negative reflex in the form of rotation of eyeballs in the direction of head and trunk tilt was demonstrated in 9 out of 100 tested patients. This reaction was observed in the patients during the period preceding a vestibular crisis or after termination thereof. A diminished negative reflex and change to a positive one was demonstrated by clinicians as a result of therapy.

At the same time, the clinical observations cannot serve as a complete analogy to explain the findings on cosmonauts, since we also observed a negative reflex with good endurance of flights, in the absence of any manifestations of vestibular dysfunction.

The rather frequent changes in perception of spatial coordinates can probably be attributed to impairment of coordinated function of sensory systems, change in afferent impulsation from the otolith system and other gravireceptors, first due to the effect of weightlessness and then to that of earth's gravity.

The nature of postflight changes in vestibular function is indicative of involvement not only of peripheral, but central vestibular structures in the observed changes, as well as integrative mechanisms of the brain. We cannot rule out the possibility of change in regulatory mechanisms of the central nervous system, neurohumoral factors, blood and spinal fluid dynamic changes in development of the systemic adaptive reaction (including that of the vestibular system) to flight factors and postflight reaction to earth's gravity.

It is imperative to conduct neurophysiological studies during space flights, first of all on animals, in order to disclose the mechanisms of seasickness in weightlessness.

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PROBABILITY OF CAISSON DISEASE AFTER PRESSURE DROP FROM 840 TO 308 MM HG

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 16 Apr 81) pp 26-28

[Article by A. S. Barer, M. I. Vakar, G. F. Vorob'yev, L. R. Iseyev, S. N. Filipenkov and V. I. Chadov]

[English abstract from source] The decompression from the hyperbaric air atmosphere with the pressure 840±5 mm Hg and subsequent 40 min exposure to the hypobaric atmosphere 308±1 mm Hg containing 40 to 95% O_2 cause a decompression disease in 5-40% cases. The probability of the disease depends on the duration of nitrogen saturation at an increased pressure, physical fitness and individual susceptibility to decompression sickness.

[Text] Decompression from a hyperbaric air atmosphere to hypobaric conditions is of definite theoretical and practical significance to altitude physiology [1-4]. We studied here the mode of decompression to a pressure of 308 mm Hg after exposure for 2-12 h to a hyperbaric air atmosphere at a pressure of 840 mm Hg. Our objective was to determine the effect of additional saturation of the body with nitrogen in the presence of elevated air pressure on probability of caisson disease [altitude decompression sickness] (CD) after changing to an absolute pressure of 308 mm, which is relatively safe in decompression from normal earth atmosphere [5-8].

Methods

A total of 43 volunteers 22-43 years of age, who had previously worked in an atmosphere rarefied to 290-310 mmHg with decompression from earth's conditions, participated in this study. Four of these subjects had a higher predisposition to CD and when working under the above conditions presented symptoms of the disease at an individual frequency of 1.7 to 4.7%.

During this study we made continuous records of the main physiological parameters (EKG, pulse and respiration rate) and monitored microclimate parameters: absolute pressure (P), partial gas pressures (pO_2, pCO_2, pN_2), air temperature (T) and relative humidity (RH). We made discrete determination of gas and energy metabolism parameters under hyperbaric and hypobaric conditions, with measurement of expenditure of energy (EE).

Each series of tests consisted of the following stages: compression from atmospheric to elevated pressure within 0.5-1 min; hyperbaric conditions for 2 to 12 h, with

$P = 840 \pm 5$ mm Hg ($pO_2 = 162.0 \pm 1.5$ mm Hg, $pN_2 = 662.7 \pm 1.5$ mm Hg, and the rest H_2O and CO_2), T from 25 to 30°C, RH from 40 to 80%; exercise in the form of rising on 27-cm step 15 times/min and EE from 200 to 240 kcal/h during the first and last hour of exposure; decompression to $P = 308 \pm 1$ mm Hg within 2-3 min; hypobaric conditions for 2 h with $P = 308 \pm 1$ mm Hg in a gas atmosphere containing 40% O_2, 60% N_2 ($pO_2 = 116.8 \pm 1.1$ mm Hg, $pN_2 = 170.2 \pm 1.0$ mm Hg), or 95-100% O_2 ($pO_2 = 299.1 \pm 1.8$ mm Hg, $pN_2 = 8.0 \pm 1.2$ mm Hg) with T from 25 to 27°C, RH from 40 to 60%, in a state of relative rest with EE from 80 to 90 kcal/h or exercise in the form of stretching a chest developer with exertion of 10 kgf over a distance of 1-1.5 m at the rate of 15-20 times per minute with average EE of 150 to 180 kcal/h during continuous exercise and 120 to 140 kcal/h when alternating 10-min periods of exercise and rest; recompression upon termination of the test within 5-10 min to atmospheric pressure; when symptoms of CD persisted we changed pressure to 2280 mm Hg using therapeutic modes of hyperbaric oxygenation [9, 10]. CD was diagnosed on the basis of subjective sensations and objective clinical symptoms, with due consideration of localization, time of appearance, ambient pressure that curbed them during recompression. The severity of CD was rated as follows: grade I--transient or mild discomfort; grade II--moderate pain that did not prevent performance of exercise; grade III--intensive pain precluding exercise; grade IV--disorders requiring immediate medical attention.

Results and Discussion

The principal results of our studies, which are listed in the Table, were indicative of a high probability of CD in all series of tests. Symptoms of this disease developed in the 41st-102d min of exposure to hypobaric conditions in 13 out of 43 subjects (30.2%) in 14 out of 74 tests (18.9%). Six tests (8%) were terminated prematurely in the 55th-96th min of exposure to 308 mm Hg due to development of grades III-IV CD in 5 cases and upon request of the subject in the presence of the cutaneous form of CD in 1 case.

Muscle and articulation pain localized chiefly in the hands appeared during exercise in 12 cases. In two cases, there was development of the isolated cutaneous form of CD in the form of eruptions on the hands and abdomen. Grade I-II muscle and joint pain usually disappeared spontaneously after discontinuing exercise. However, when exercise was continued under hypobaric conditions there was periodic recurrence of local discomfort, which disappeared entirely only upon recompression to 350-530 mm Hg. The cutaneous form of the disease was curbed only at a pressure of 700-760 mm Hg. Recompression to hyperbaric conditions was not needed in any of the cases of CD.

Continuous 2-h exercise at a pressure of 308 mm Hg led to development of the disease in 20-40% of the cases (see Table, series I-II.1), depending on duration of the period of nitrogen saturation under hyperbaric conditions. A decrease to one-half in exercise by alternating 10-min periods of exercise and rest lowered the incidence of CD to 14.3% (see Table, series II.2). The change from an oxygen-nitrogen atmosphere containing 60% nitrogen to pure oxygen with no more than 5% N_2 content in the space under the mask did not prevent CD, since the incidence thereof constituted 12.5% when exercising with EE of 120 to 140 kcal/h (see Table, series III), and it showed virtually no difference from incidence of CD (series II.2).

With 2-h exposure to pressure of 308 mm Hg in a state of relative rest (see Table, series II.3), CD was observed in only 1 case (5%) in a subject who had a history of increased predisposition for this disease. Apparently, prior screening for

resistnace to decompression from normal atmosphere to a pressure of 290-310 mm Hg would have ruled out CD under the tested conditions at rest. In four subjects with increased susceptibility for the disease, who participated in the first and second series of tests (see Table), CD was demonstrated in four out of five cases (80%). This exceeds significantly the individual incidence of CD observed in the same subjects with decompression to 290-310 mm Hg from normal atmospheric pressure.

Range of tests, incidence of CD and distribution thereof according to severity, initial localization, time of appearance of symptoms and pressure at which they were curbed

Test series	Cases of CD during studies	Grade of CD				Initial localization								Time of appearance of symptoms, min	P curbing symptoms, mm Hg			
		I	II	III	IV	skin	arm	elbow joint	forearm	wrist	finger	thigh	knee joint		350–380	405–463	508–530	700–760
I. 2 h 840 mm Hg and 2 h 308 mm Hg (40% O_2, 60% N_2)	1/5			1			1							68	1			
II. 12 h 840 mm Hq and 2 h 308 mm Hq (40% O_2, 60% N_2)																		
II.1. EE 150-180 kcal/h	8/20	4	2	1	1	1	4				1	1	1	41—102	4	3		1
II.2. EE 120-140 kcal/h	3/21	1	1	1			1	1		1				48—95		1	2	
II.3. EE 80-90 kcal/h	1/20	1				1								63				1
III. 12 h 840 mm and 2 h 308 mm Hg (95-100% O_2) with EE 120-140 kcal/h	1/8				1				1					57		1		
Totals	14/74	6	3	3	2	2	6	1	1	1	1	1	1	41—102	5	5	2	2

Note: Number of subjects who developed CD is given in the numerator and number of subjects tested in the denominator.

It is quite obvious that the increase in incidence of symptoms among individuals susceptible to CD and development of the disease in subjects who had not suffered from it previously is attributable to exceeding the safe level of saturation of the body with nitrogen in a hyperbaric air atmosphere. This is also confirmed by extrapolation of a number of modes of safe decompression following immersion in water [11, 12] to hypobaric conditions. The estimates referable to decompression from an air atmosphere at a pressure of 840 mm Hg indicate that 330-380 mm Hg is a safe level of pressure, which is 20-70 mm Hg higher than the pressure mode used in our case. However, the minimal safe pressure for decompression from a

hyperbaric air atmosphere (P = 840 mm Hg) requires further checking, since our study revealed that the incidence of CD depended substantially on individual predisposition and physical activity of the subjects.

Thus, exposure of man to hypobaric conditions (P = 308±1 mm Hg) for more than 40 min after decompression from a hyperbaric air atmosphere (P = 840±5 mm Hg) often leads to development of CD, the probability of which depends on both the level of physical activity and individual predisposition for this disease.

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ION REGULATING FUNCTION OF HUMAN KIDNEYS DURING LONG-TERM SPACE FLIGHTS AND IN MODEL STUDIES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 16 Jun 81) pp 29-33

[Article by A. I. Grigor'yev, B. R. Dorokhova, G. S. Arzamazov and B. V. Morukov]

[English abstract from source] Ten cosmonauts who performed 30- to 175-day space flights onboard Salyut-4 and Salyut-6, and 50 test subjects exposed to head-down tilt (-4°) for 182 days were examined. In actual and simulated weightlessness renal excretion of calcium and potassium increased, reaching maximum during the 4-6th weeks. Before and after flight the test subjects were exposed to loading salt tests. Renal excretion of calcium and potassium in response to the loading tests with their salts postflight was much higher than preflight. During the potassium chloride load the aldosterone content in blood correlated with potassium excretion, and during the calcium lactate load an increase in calcium excretion was paralleled by a decrease in the parathormone content in blood. It is most likely that the negative balance of ions in weightlessness is associated with the reduced capacity of tissues to retain electrolytes due to the decreased ion pool. It was shown that electrolyte balance can be beneficially influenced by exercise.

[Text] Marked changes in electrolyte metabolism have been demonstrated with increase in duration of space flights [1-3]. It was deemed important to determine whether these changes would progress with longer exposure of man to weightlessness and to what extent changes in the functional state of the kidneys are involved in increased electrolyte excretion. It was therefore necessary to examine the role of the kidneys and their regulatory systems in the occurring disorders of ion metabolism.

Methods

We examined 10 cosmonauts who had participated in space flights lasting 30 to 175 days. Since major difficulties are involved in examining metabolism during space flights, renal function was also studied in 50 men who had been kept in head-down [antiorthostatic] position (-4 to -6°) during bed rest for 30 to 182 days.

Ion regulating renal function before and after space flights, as well as at different stages of immersion and bed rest was evaluated by means of calcium chloride

and calcium lactate loading tests. The dosage of salts given per os constituted 0.75 and 0.50 meq/kg body weight, respectively. The method of performing water-ion loading tests and criteria for rating the results of the tests were described previously [4-6].

All of the tests were conducted against a background of measured salt and fluid intake. We used both absolute values for excretion of fluid and electrolytes, and percentage of renal excretion thereof [7].

Determination was made of concentrations of sodium and potassium by flame photometry, calcium and magnesium by spectrophotometry on an atomic absortiometer, chlorides by titrometry using a Radiometer chloride meter, ionized calcium by direct potentiometry with an ion-selective electrode, creatinine by spectrophotometry (SF-4) with the Jaffe reaction with picric acid in samples of blood serum or plasma, as well as urine. Blood hormone activity was measured by means of standard test kits: aldosterone (Aldon ^{3}H), insulin (Insin ^{125}I) and parathyroid hormone (PTH ^{125}I).

The obtained data were processed by methods of variation statistics on an M-220 computer and by means of the PRALG/EVM YeS dialogue system using special programs prepared jointly with V. K. Vasil'yev and L. A. Rustam'yan.

Results and Discussion

No appreciable changes were demonstrated in blood ion concentration on the first day after space flights. There was merely some decline of potassium content and increase in fraction of ionized calcium, which was indicative of efficacy of homeostatic mechanisms. However, the electrolyte composition of blood serves as an accurate reflection of ion content only in the bulk of extracellular fluid, but does not permit evaluation of electrolyte balance, since it is possible to maintain a normal level thereof in blood for some time, even with a negative balance, at the expense of mobilizing deposited ions. For this reason, it was important to examine the mechanisms involved in maintaining a stable ion concentration in blood under such conditions and, first of all, to study the role of the kidneys, including demonstration of electrolyte excretion.

There was considerable increase in calcium excretion and, to a lesser extent, potassium excretion by most cosmonauts following long-term space flights. We had to determine when these changes occurred, during or after the space flight. Analysis of urine specimens collected in weightlessness revealed a relative increase in renal excretion of osmotically active substances, potassium and calcium. Maximum increase in elimination of electrolytes was noted by the end of the first month of a space flight. There was no further increase in these changes thereafter. Analogous results were obtained from analysis of urine specimens collected from the cosmonauts aboard Gemini 7 and Skylab in flight [8, 9]. Excretion of these electrolytes was considerably greater than intake thereof with food, as a result of which there was a decrease in levels of these ions in the body [10].

A more detailed study of the dynamics of electrolyte excretion and its relation to nature of salt intake with food was conducted in model experiments. It was established that the increase in kaliuresis usually started on the 10th-15th day of bed rest and reached a maximum on the 20th-50th day. After the maximum increase in potassium excretion, there was undulatory change at subsequent stages of bed rest, but even when kaliuresis diminished it was above the base level. At virtually all

stages of bed rest, when there was increased potassium excretion, there was an increase in blood aldosterone activity (r = +0.92). This was sometimes associated with an increase in sodium excretion. Analogous changes had been demonstrated in weightlessness also [10], which is indicative of the possible influence of aldosterone on potassium secretion independently of its antinatriuretic action.

On the basis of studies, in which a record was kept of potassium content in the diet, it can be concluded that the observed increase in renal excretion of potassium during bed rest was the consequence of hypokinesia. Analysis of the obtained data warranted the assumption that the negative balance when motor activity is restricted, in weightlessness, as well as during bed rest and immersion, was based on the fact that it was impossible for this ion to be retained in the body, probably due to a decrease in capacity of the potassium reservoir in muscle tissue cells. Under these conditions, the change in activity of mineralocorticoids was secondary.

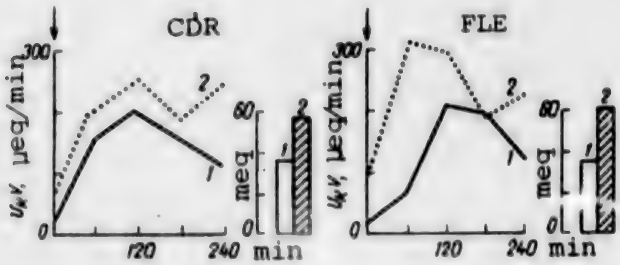

Figure 1.
Rate of K excretion and total renal elimination thereof in 4 h in KCL loading test after 175-day space flight. Here and in Figure 3:
1) preflight
2) postflight
Arrows show start of loading test

This hypothesis was confirmed in studies using the potassium chloride loading test. There was an increase in potassium excretion during the test in both cosmonauts on the 2d and 4th days after the 175-day flight, as compared to background levels (Figure 1).

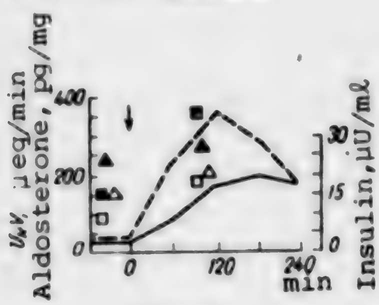

Figure 2.
Rate of renal excretion of K (curves), concentration of aldosterone (squares) and insulin (triangles) in blood after KCl loading before and during bed rest. Solid line, white squares and triangles--control; dotted line, black squares and triangles--158th day of bed rest

An analogous increase in rate of potassium excretion (U_KV) after KCl loading was observed during prolonged bed rest (Figure 2), and elimination of potassium during the loading test was greater at all stages of hypokinesia than in the background (BG) period, which was related to a change in transport of this ion in tubules, rather than increase in its filtration charge. The most probable cause of increased potassium excretion during bed rest was increased secretion thereof in the distal segment of the nephron. Evidently, the distal tubules were important in this respect, since the collecting tubules had an appreciable effect on kaliuretic function only when there was an excess of this ion in the body, whereas during bed rest a potassium deficiency was noted.

In view of the fact that the state of hormonal regulation plays an extremely important role in tubular transport of potassium, determination was

made of aldosterone and insulin concentrations in blood serum before and 1.5 h after KCl loading at different stages of bed rest. It was established that blood aldosterone content during the test was higher at all stages of bed rest than in the BG. The concentration of aldosterone increased even more 1.5 h after the loading test (see Figure 2), although the degree of increase was virtually the same as in the BG. Maximum aldosterone content after the test was noted in subjects who presented a large increase of U_KV. There was a stronger relationship between the increase in rate of renal excretion of potassium and increase in blood aldosterone concentration during bed rest than in the BG. Blood insulin activity after the loading test increased on the 78th and 158th days of bed rest, as in the BG period.

Apparently, the increased secretion of aldosterone after delivery of a potassium excess into the body leads to increased excretion thereof to counteract development of hyperkaliemia, and this increases potassium tolerance. The increase in insulin secretion, which is instrumental in passage of potassium into cells, serves the same purpose [11]. Blood insulin activity after the loading test increased less during bed rest than in the BG, but absolute values thereof were considerably higher than base levels. Increased production of insulin has a direct effect on potassium transport in renal tubules [12, 13].

Impairment of calcium metabolism is also one of the adverse manifestations of weightlessness and prolonged restriction of motor activity. There was gradual increase in renal excretion of calcium, usually up to the 20th-35th day of immersion and bed rest, after which this parameter became stable, remaining elevated to the end of exposure to these factors. Calcium excretion was 2-5 meq/day (average 3.4 meq/day) higher during 182-day bed rest than in the BG. During the entire period of hypokinesia, the kidneys excreted 500-800 meq more calcium than in the same time with ordinary motor activity. However, this did not signify that calcium excretion was the same at all stages of bed rest. There was somewhat greater excretion during the 2d month of bed rest and somewhat lesser excretion during the 4th-5th month of bed rest. On the average, monthly renal excretion of calcium during bed rest lasting 6 months was slightly over 100 meq more than in the base period.

It was established that not only the absolute amount of calcium excretion, but level thereof in relation to intake with food increased during bed rest. During 182-day bed rest, renal excretion of calcium increased to 30-39%, versus the base level of 18-24%. The increase in calciuresis could have been the consequence of diminished mineralization of osseous tissue, which was observed in this experiment [15], and increase in concentration of ionized calcium in blood, which ultimately led to an increased load on the nephron and, consequently, increase in calcium excretion.

An increase in calcium excretion was also observed with the loading tests. In the water loading test (20 mℓ/kg weight) calcium excretion was considerably greater after long-term space flights than before flights, and while calcium excretion increased to virtually the same extent, by 1.8-2.2 times, after 30- and 63-day flights, it increased by almost 5 times after the 96-day space flight.

Calcium lactate loading tests were performed to determine the mechanisms of change in calcium metabolism under these conditions. In this test, calcium excretion in urine on the 2d day after a 140-day flight exceeded the preflight level (Figure 3). Blood serum ionized calcium increased from 1.04 mM/ℓ (BG) to 1.28 mM/ℓ in the commander (CDR) and from 1.12 to 1.35 mM/ℓ in the flight engineer (FLE). There was, however,

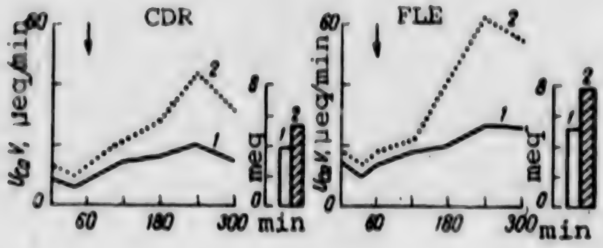

Figure 3.
Rate of calcium excretion and total renal elimination thereof in 4 h during calcium lactate loading test after 140-day space flight

no change in filtration charge of calcium, as compared to base value, which was indicative of the important role of reabsorption of calcium in the tubules to changes in ion regulation.

Analogous changes in calcium metabolism were demonstrable in model experiments, where the calcium lactate loading test was performed not only after, but during bed rest. At all tested periods (42d, 82d and 166th days of hypokinesia) postloading calcium excretion was greater than in the BG (Figure 4).

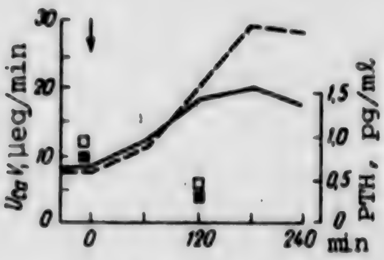

Figure 4.
Rate of renal calcium excretion (curves) and PTH concentration (squares) in blood after calcium lactate loading test before and during bed rest. Solid line and black squares--control; dotted line and white squares--82d day of bed rest

Absolute reabsorption of calcium after giving calcium lactate was lower than in the BG, but did not differ appreciable from preloading levels at the same stage of hypokinesia. However, relative calcium absorption was lower after the loading test during bed rest than after the same test in the BG, and it was lower than before the tests at the same stages of bed rest. On the 82d and 166th days of bed rest, the minimal levels of relative calcium absorption reached 87.6±1.9 and 89.2±0.6%, respectively, which was considerably lower than when tested in the BG period (92.4±0.7%; $P<0.05$). Consequently, with increase in duration of bed rest the decline in calcium reabsorption in tubules was of decisive significance to increased calcium excretion, rather than change in its filtration charge.

In order to determine the significance of hormonal regulation to changes in calcium transport during long-term bed rest, we determined the blood serum concentration of parathyroid hormone (PTH) in 6 subjects at different stages of 182-day hypokinesia, before and after loading tests. We observed a drop in PTH content (see Figure 4) after calcium lactate loading during bed rest, as in the BG period, which could have been the cause of diminished reabsoprtion of calcium in renal tubules and, consequently, of increased excretion thereof.

The results of these studies enabled us to establish that the changes in ion metabolism in weightlessness are attributable primarily to metabolic distinctions, which lead to a decrease in tissular capacity to retain ions, and concomitant changes in the endocrine status.

There was theoretical validation of the principles and choice of means of correcting the disorders on the basis of the demonstrated causes of changes in electrolyte

homeostasis and mechanisms of change in ion transport in the kidneys. During long-term flights, they were based on counteracting the diminished load on the skeletomuscular system. In the model experiments (49- and 182-day bed rest), we studied the effects of two modes of physical conditioning differing in nature, duration and loads. The conditioning methods have been described in detail in special publications [14-16].

These studies revealed that renal excretion of potassium and calcium was reliably lower in subjects who engaged in intensive exercise during bed rest than in the control group, intake thereof being the same in both groups. We demonstrated a reliable correlation between changes in ion excretion, extent and scope of exercise. When the intensity of working out was significantly diminished, renal excretion of calcium and potassium was only slightly lower than in the control. With increase in amount and intensity of exercise there was decrease in ion excretion. At the same periods, activity of blood aldosterone, cortisol and particularly PTH increased to a lesser extent than in the control.

On the basis of our findings, it can be assumed that there was less marked decrease in capacity of tissular ion depots when exercising than during hypokinesia. The results of calcium and potassium salt loading tests can serve to confirm this. The rate of ion excretion was considerably lower after these tests than in the control, whereas with regular exercise it differed little from BG levels. In assessing hormonal regulation of fluid and ion metabolism, it must be noted that changes therein were qualitatively the same as in the control, but usually less marked and differed less from BG findings.

Thus, exercise, which increased the load on the skeletomuscular system, diminished significantly the changes in electrolyte metabolism that are observed in man during prolonged bed rest. However, we did not succeed in eliminating entirely the hyperexcretion of ions with the exercise modes we used. Additional administration of salts also failed to replace the electrolyte deficiency, which occurred during long-term restriction of motor activity, since the change in hormonal regulation under these conditions was directed toward increasing elimination thereof to maintain the appropriate ion homeostasis, primarily in blood.

Further investigation of mechanisms of changes in electrolyte metabolism and prevention of shortage thereof during long-term flights is one of the most important tasks for space medicine.

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STRUCTURAL AND FUNCTIONAL PROPERTIES, AND ENERGY METABOLISM OF ERYTHROCYTES DURING SPACE FLIGHTS VARYING IN DURATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 28 Jan 81) pp 34-37

[Article by A. S. Ushakov, G. I. Kozinets, S. M. Ivanova and V. P. Matviyenko]

[English abstract from source] The structural and functional properties and energy metabolism of erythrocytes in peripheral blood of crew members who performed space flights of varying duration were investigated. Certain changes in the morphology, function and energy metabolism of erythrocytes were seen after long-duration space flights.

[Text] There are changes in function of a number of systems and organs under the influence of space flight factors, and they reflect changes in ambient parameters. Some changes are also observed in blood. During flights and in the readaptation period there are changes in hemoglobin content per cubic mm, quantity of erythrocytes, reticulocytes and erythropoietin level [1, 2].

We submit here the results of a complex study of structural and functional properties, as well as energy metabolism of peripheral blood erythrocytes of cosmonauts who had participated in space flights of varying duration.

Methods

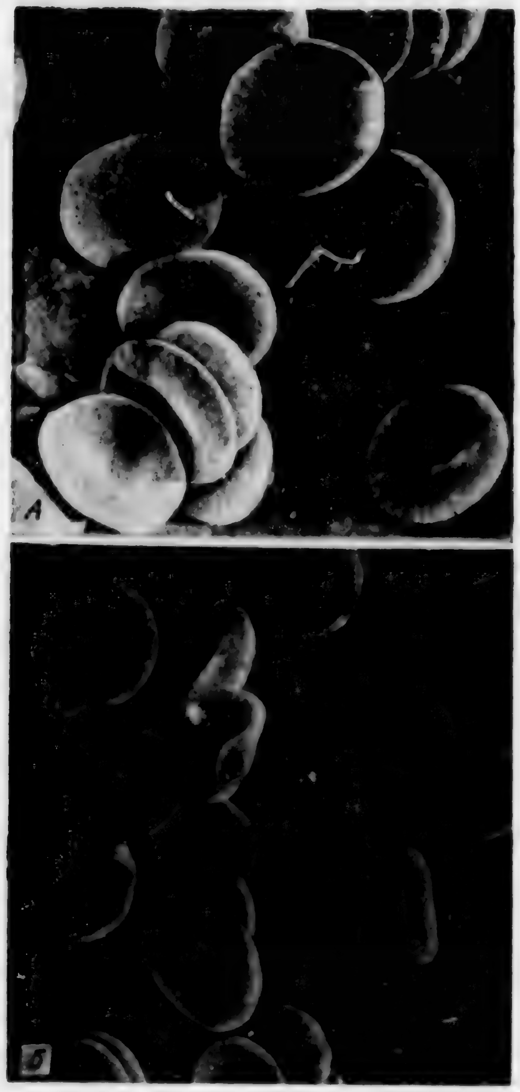
Samples of peripheral blood of cosmonauts served as the material of our study; they were collected at different times after completing space flights lasting 7, 8, 30, 63, 96, 140 and 175 days.

Scanning electron microscopy [3], interference microscopy [4], analytical electrophoresis of erythrocytes [5] and preparative electrophoresis of erythrocytes [6] were used in the cytological studies.

Examination of energy metabolism included assays of adenosine triphosphate (ATP), 2,3-diphosphoglyceric acid (DPG), reduced glutatione, intensity of glycolysis and activity of the enzymes, lactate dehydrogenase (LDH) and glucose-6-phosphate dehydrogenase (GPDH).

ATP content was assayed by enzymospectrophotometry. We assessed intensity of glycolysis by the increment of lactic acid in erythrocytes incubated at T = 38°C for

2 h. The enzymospectrophotometric method was used to assay produced lactic acid, Sigma Co kits (No 35-UV, 1974) were used to assay DPG. Reduced glutathione was examined using Elman's reagent [7]; LDH activity was determined by the method of Wu and Racker [8]; GPDH activity was determined by the Kornberg method [9].



Electron microscopic appearance of form of erythrocytes after 8-day (A; magnification 2800×) and 140-day (Б; magnification 2500×) flights

Results and Discussion

Examination of the form and superficial architectonics of erythrocytes by the method of scanning electron microscopy revealed that space flights lasting up to 8 days did not elicit changes in ultrastructure of erythrocytes. Discocytes constituted 87-89%, discocytes with one process 1.5-2.8%, crenated discocytes 3.5-4.5%. Discocytes with multiple processes, dome-shaped erythrocytes, erythrocytes in the form of a mulberry, deflated ball, and spherocytes totalled about 5-6%, and degeneratively altered cells about 0.5%. These figures are consistent with standard physiological parameters (see Figure, A).

Table 1. Quantitative distribution (%) of erythrocytes according to shape in the crew of the first (96-day flight) and second (140-day flight) mission aboard the Salyut-6 orbital station

Shape of erythrocytes	First crew				Second crew							
	7th day		33d day		preflight		1st day		25th day		41st day	
	postflight						postflight					
	CDR	FLE	CDR	FLE	CDR	FLE	CDR	FLE	CDR	FLE	CDR	FLE
Discocytes	52,0	59,0	83,5	81,5	87,0	93,0	86,5	89,5	92,0	90,0	96,0	95,0
Discocytes with one process	6,0	6,0	5,0	2,0	2,5	1,5	2,5	1,0	1,0	1,0	1,0	1,0
Crenated discocytes	6,0	9,0	2,0	2,5	3,0	1,0	3,5	2,0	3,0	5,0	2,0	3,0
Discocytes with numerous processes	7,5	8,5	3,6	6,0	3,5	1,0	0,5	1,0	0,5	0	0	0
Dome-shaped erythrocytes	3,5	1,5	1,5	2,5	2,0	2,5	3,0	4,5	3,0	2,0	0	0
Mulberry-shaped erythrocytes	3,5	5,0	0	1,0	0	0	0	0	0	0	0	0
Erythrocytes in the form of deflated ball	3,5	3,5	1,1	1,0	1,5	0,5	2,5	2,0	1,0	1,0	0,5	1,0
Spherical erythrocytes	3,5	4,0	0,5	1,0	0	0	0	0	0	0	0	0
Degeneratively altered and destructed erythrocytes	5,0	3,5	2,5	2,5	0	0,5	1,5	1,0	0,1	1,0	0	0
Pathological erythrocytes	9,5	0	0,5	0	0,5	0	0	0	0	0	0,5	0

Note: Additional studies were not performed on members of the first crew.

Most cells were represented by discocytes in both crew members on the 7th day after returning from the 96-day space flight. However, the flight engineer (FLE) presented isolated cells with altered configuration: in the form of a droplet, sickle, jelly fish. The distribution of erythrocytes corresponded to the normogram on the 33d postflight day (Table 1).

There was a negligible increase in dome-shaped erythrocytes and cells in the form of a deflated ball (see Figure, Б and Table 1) in cosmonauts who participated in the 140-day flight 1 day after landing. No changes in shape of erythrocytes were observed on the 25th and 41st postflight days.

Examination of distribution of erythrocytes according to dry mass, performed by the method of interference microscopy, revealed that flights lasting up to 8 days did not elicit deviations from normal findings.

Table 2. Parameters of energy metabolism in blood erythrocytes of crew of first mission aboard Salyut-6 orbital station (96 days)

Parameter	Preflight		Postflight					
			1st day		7th day		30th day	
	CDR	FLE	CDR	FLE	CDR	FLE	CDR	FLE
ATP, μM/mℓ erythrocytes	0.62	0.85	0.29	0.49	0.45	0.62	0.98	1.06
Glycolysis, μ/M lactic acid/mℓ erythrocytes	2.60	2.04	0.94	3.50	2.61	3.89	2.50	2.45
LDH activity, μM NAD•H_2/mℓ erythr.	4.66	3.20	3.99	3.92	4.11	4.03	4.30	4.58
GPDH activity, μM NADP•H_2/mℓ erythrocytes	1.06	0.93	1.44	1.33	1.03	1.06	1.09	1.32

Examination of cosmonauts who had participated in long-term space flights revealed that their dry erythrocyte mass remained in the range of physiological fluctuations. Studies of individual dynamics of these parameters showed that there was an increase in number of cells with large mass in the CDR on the 33d day after the 96-day flight. On the 1st day after the 140-day flight, both crew members presented an increase in percentage of erythrocytes with low mass.

Examination of mean erythrocyte volume, which was conducted using a Coulter counter, revealed that cell volume diminished somewhat on the 1st day after long-term flights. Thus, mean erythrocyte volume constituted 72.5 μm^3 in the CDR and 74.6 μm^3 in the FLE after the 140day flight, versus the normal of 80-96 μm^3. There was restoration of base values by the 25th day of the readaptation period.

Studies of electrophoretic mobility of erythrocytes revealed that there were varying degrees of decrease in mobility, to 0.965-0.994 μm•cm/V•s on the first day after short- and long-term flights. The base values were in the range of 1.035-1.138 μm•cm/V•s. On the 3d day electrophoretic mobility of erythrocytes conformed to normal values.

Preparative electrophoretic separation of erythrocytes on the first day after both short- and long-term flights revealed widening of the distribution curve, which was indicative of some heterogeneity of erythrocyte charge.

Studies of energy metabolism of erythrocytes showed that brief flights elicited no changes in the parameters of energy metabolism that we determined.

Changes of an inadequate nature in energy metabolism parameters were noted as a function of flight duration in studies thereof during longer missions. As was reported previously, examination of cosmonauts referable to the first and second crews of the Salyut-4 orbital station (after completion of 30- and 63-day missions) revealed a tendency toward diminished glycolytic activity in the crews of both missions on the first day after landing [10].

Table 3. Energy metabolism in blood erythrocytes of members of second and third crews of Salyut-6 orbital station

Parameter	Preflight				Postflight								Physiological norm
	2d crew		3d crew		second crew				third crew				
					1st day		25th day		1st day		28th day		
	CDR	FLE	CDR	FLE	CDR	FLE	CDR	FLE	CDR	FLE	CDR	FLE	
ATP content, μM/g Hb	6.26	5.95	7.85	6.13	4.24	3.21	7.10	5.90	4.75	3.74	5.12	5.19	5.63±0.29
Glycolysis (increment of lactic acid, μM/g Hb)	5.12	6.03	5.05	5.35	4.53	4.20	6.65	5.66	8.39	6.93	10.08	9.53	7.28±0.26
LDH activity, μM NAD·H_2/g Hb	26.12	21.85	27.34	24.0	21.55	16.01	29.48	20.52	22.25	29.91	36.14	33.0	24.85±0.46
GPDH activity, μM NADP·H_2/g Hb	3.92	3.28	3.76	4.42	2.83	2.57	2.77	4.11	3.87	5.60	6.28	3.88	4.37±0.39
Reduced glutathione, μM/g Hb	—	—	8.09	10.10	—	—	—	—	6.73	11.58	8.85	7.50	9.81±0.48
DPG, μM/g Hb	—	—	—	—	—	—	—	—	9.74	10.92	19.79	14.6	12.80±2.30

Note: Mean data on 12 subjects are listed.

Examination of erythrocyte metabolism after completion of the 96-day flight revealed significant decline of ATP content in both crew members (by 50% in the CDR and 60% in the FLE; Table 2). In this case, intensity of glycolysis was increased, as compared to preflight levels. Concurrently, we observed an increase in LDH activity. ATP level rose on the 7th postflight day, but did not reach preflight values. On the 30th day, all of the tested parameters were in the normal range and showed virtually no different from preflight values.

Examination of energy metabolism of erythrocytes after the 140-day flight showed a decrease in intensity of metabolism in both crew members on the 1st postflight day (Table 3). The decrease in ATP and intensity of glycolysis constituted 33 and 12%, respectively, in the CDR, 47 and 32% in the FLE. On the 25th day, the values of tested parameters showed virtually no difference from preflight findings.

The nature of changes in intensity of energy metabolism of erythrocytes following the 175-day flight was analogous to that demonstrated after the 96-day mission. There was a decline of ATP level against a background of increased glycolytic activity. On the 8th postflight day there was an increase in intensity of glycolysis, rise in DPG content and increase in LDH activity, as compared to the findings on the first postflight day and base values (see Table 3).

The demonstrated changes in energy metabolism (decline of ATP and increase in glycolytic activity) are probably related to triggering of compensatory mechanisms in response to the effects of space flight factors, and they are directed toward preserving the structural integrity of cells. On the whole, the obtained data indicate that short-term flights lasting up to 8 days do not elicit appreciable changes in structural and functional, as well as metabolic parameters of erythrocytes. Long-term space flights are associated with a number of morphofunctional changes and

some alteration of energy metabolism of erythrocytes. The insufficient volume of studies does not enable us to derive a definitive conclusion as to the physiological significance of these changes; however, there are grounds to believe that the observed changes are not pathological, but adaptive in nature.

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POSITIVE PRESSURE BREATHING AS A MEANS OF PREVENTING ADVERSE REACTIONS TO ANTIORTHOSTATIC POSITION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan Feb 82 (manuscript received 27 Jan 81) pp 38-40

[Article by V. G. Voloshin, V. A. Karpusheva, B. F. Asyamolov, R. A. Bondarenko and V. S. Panchenko]

[English abstract from source] The experiments in which 15 healthy male test subjects were exposed to head-down tilts at -15° and -30° demonstrated that the central and cerebral circulation can be normalized by a positive pressure breathing of 15-20 mm Hg with a partial compensation.

[Text] Positive pressure breathing (PPR), which is used extensively in aviation medicine, elicits a number of changes in the cardiorespiratory system.

It diminishes venous return to the heart due to deposition of blood in the periphery [1, 2]. Systolic (SV) and minute (MV) volumes of the heart decrease, as do cerebral circulation and blood volume in the lungs [1-5], and there are changes in phase structure of cardiac function [4].

Such hemodynamic changes are also inherent in the orthostatic test. For this reason, efforts were made to use PPR to develop orthostatic stability in immersed subjects [5, 6].

We were impressed by deposition of blood in the limbs and diminished circulating volume thereof with PPR, which could theoretically normalize intracranial hemodynamics in simulating the hemodynamic effects of weightlessness by using an antiorthostatic [head tilted down] position (AOP) [7]. Our study was pursued to test this hypothesis.

Methods

We conducted 23 studies involving 15 healthy men 19-23 years of age. The hemodynamic effects of the acute period of adaptation to weightlessness were simulated in the first series of studies by means of 30-min AOP at an angle of -30° (short-term model) and in the second series by AP at an angle of -15° for 3 h 50 min (long-term model).

In the first series of tests, the subjects breathed oxygen at excess pressure of 20, 30, 35 and 25 mm Hg between the 6th and 25th min of AOP, for 5 min in each mode.

In the second series, excess pressure in the lungs of 20-30-15 mm Hg, for 10 min in each mode, and for 5 min at 10 mm Hg was created 1 h after AOP at an angle of -15°. Three cycles of this procedure were performed at 30-min intervals.

A KPT-1 oxygen instrument and GSh-6 helmet were used for PPR. The elevated intrapulmonary pressure was compensated by counterpressure to the head, neck and trunk region (chest and abdomen) in a pneumatic gear connected with the space under the helmet, which facilitated expiration significantly, even at high levels of excess pressure [8].

During these tests, we recorded the EKG, rheoencephalogram (REG) in the bitemporal leads using a Levkoy-3M instrument. SV and MV were determined rheographically, using an RPG-2-02 tetrapolar rheograph. Arterial pressure (AP) was measured according to Korotkov with correction for level of excess pressure.

The state of cerebral circulation according to pulsed filling of the head (PFH) [9] and dicrotic index (DCI) served as the main criterion of effectiveness of PPR.

Results and Discussion

In both series of tests, the values of the parameters under study obtained when breathing with oxygen at normal pressure in horizontal position, taken as 100%, served as the background.

By the 5th min in AOP in the first series of tests, there was time for all of the clinical symptoms to develop that were attributable to redistribution of blood in the upper half of the body. The subjects complained of heaviness of the head, difficulty in breathing through the nose, pulsation in the temples and hoarseness. External signs included hyperemia of the face and upper third of the trunk, vascular pulsation in the neck region and some puffiness of the face.

As compared to background values, PFH, DCI and SV were 48.128% ($P<0.001$) and 12% ($P<0.05$) higher, respectively (Figure 1). Pulse rate was somewhat slower and AP changed insignificantly.

PPR with 20 mm Hg excess pressure elicited a positive response according to both subjective and objective data. Apparently, there was a decrease in circulating blood volume as a result of peripheral deposition of blood and manifestation of the vasoconstrictive effect of oxygen, which led to disappearance of heaviness of the head, while the angle of AOP was perceived to be smaller. Elevated pressure under the helmet also elicited some effect. Thus, in control tests with elevated pressure in the space under the helmet (breathing air at normal barometric pressure), subjectively there was some improvement in endurance of AOP, but less marked that with PPR. The configuration of the REG at excess pressure of 20 mm Hg had the same appearance as obtained with the subjects in horizontal position. PFH, DCI and SV decreased to 95, 149 and 95%, respectively (unreliable differences). PPR at 30 and 35 mm Hg caused more deposition of blood and was characterized by further decline of PFH to 93 and 85%, DCI to 142 and 136% and SV to 81 and 68% ($P<0.001$).

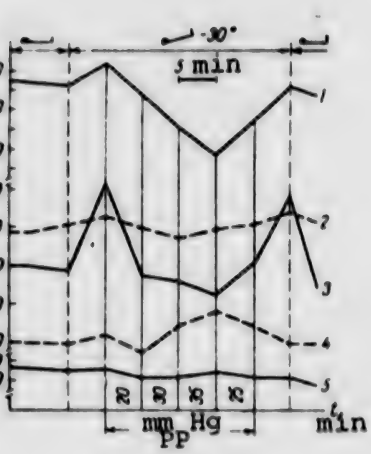

Figure 1.
Changes in SV (1; m), systolic (2) and diastolic (4) AP (mm Hg), PFH (3; %) and heart rate (5; per min) in AOP at angle of -30° with PPR

PPR at 25 mm Hg led to elevation of these parameters to 102, 161 and 84% respectively. A smooth pressure drop was associated with change in configuration of the REG inherent in AOP, elevation of PFI level to 138%, DCI to 251% and SV to 100%. At all levels of excess pressure there was no appreciable change in respiratory rate, and there were no complaints of breathing difficulty.

At the final stage, we performed brief orthostatic tests at different angles for equivalent evaluation of hemodynamic changes during PPR.

There was individual conformity of changes in physiological parameters during PPR at 30 and 35 mm Hg to those observed during orthostatic tests at 30 and 45° angles.

Thus, the results of this series of studies revealed that equalization of hemodynamic parameters to levels corresponding to horizontal position is achieved by PPR at 20 mm Hg. Breathing at excess pressure of more than 30 mm Hg elicited changes that are typical for the orthostatic test.

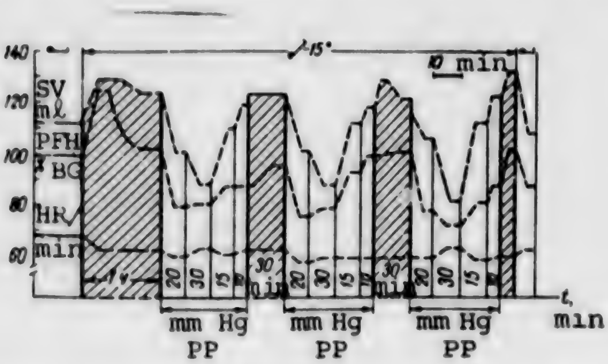

Figure 2.
Changes in SV, PFH and heart rate in AOP at angle of -15° and during PPR

In the second series of tests, by the end of the first hour of AOP the subjects reported mild symptoms of redistribution of blood to the upper half of the body; PFH constituted 102%, DCI 152% and SV was 7% above background level (unreliable differences) (Figure 2).

Already during the first cycle of PPR at 20 mm Hg the subjects reported noticeable decrease in sensation of blood rushing to the head. PFH, DCI and SV dropped objectively to 79, 142 and 86%, respectively ($P<0.05$). At excess pressure of 30 mm Hg the sensation of heavy head and facial hyperemia disappeared entirely. Some subjects developed the illusion of horizontal position when their eyes were closed.

With success decrease of excess pressure to 15, 10 and 0 mm Hg, there was gradual development of the typical symptoms of redistribution of blood, but less marked than before PPR. In conformity with excess pressure levels there was an increase in PFH to 87-95%, DCI to 179-204% and SV to 99-106%. PFH was close to the base value, while SV increased to levels recorded at the end of the first hour of AOP by the 30th min of AOP after the first cycle of PPR.

During the second and third cycles of PPR the condition of the subjects and direction of changes in parameters studied were identical to the findings in the first

cycle. Overall duration of PPR in the entire period of the study constituted 1 h 45 min, but there were no complaints of feeling worse, difficult breathing or fatigue. The results of the second series of tests indicate that less marked hemodynamic changes are curbed rather effectively by PPR at 15 mm Hg.

These studies demonstrated an inverse relationship between level of excess pressure and PFH and SV levels. They confirmed the possibility of normalization of central and intracranial hemodynamics when blood shifts to the upper parts of the body by using PPR. Excess pressure of 15-20 mm Hg was found to be effective for this purpose. PPR at 30-35 mm Hg elicited changes in the physiological parameters under study that were inherent in orthostatic tests at angles of 30-45°.

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RELATIONSHIP BETWEEN MICROFLORA AND IMMUNITY OF COSMONAUTS CARRYING STAPHYLOCOCCUS AUREUS IN THE NASAL CAVITY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 1 Jan 81) pp 40-43

[Article by T. N. Nikolayeva, Ye. V. Guseva, R. Yu. Tashpulatov and G. D. Syrykh]

[English abstract from source] The crewmembers who carried Staphylococcus aureus in the nasal cavity preflight showed an increased content of immunoglobulins IgA and IgM in the nasal cavity and that of IgM in blood serum postflight. The increased content of IgM in the nasal cavity did not depend on the size of the microbial focus in that biotope because there was no significant correlation between the two parameters.

[Text] It is of particular interest to investigate the correlations between microflora and parameters of immunity in cosmonauts who are carriers of Staphylococcus aureus. The existing microbial cenosis of the upper respiratory tract of healthy carriers of S. aureus, which is in a dynamic relationship to immunity, may be disrupted under the influence of exogenous factors. As a result, the possibility cannot be ruled out that infections will occur that are caused by conditionally pathogenic representatives of the microflora.

Man's long-term stay in a spacecraft cabin could lead to dysbacteriotic changes in state of the automicroflora of the integument, the nasal cavity, mouth and throat [1-3]. An increase in number of cells and cross-contamination of the nasal cavity by S. aureus cells, as well as significant decrease in Haemophilus sp. cells in the buccal cavity, are observed [4].

Studies of local immunity function on the basis of immunoglobulin (Ig) content of cosmonauts' tonsils after 49 days in space revealed a drastic reduction (to the extent of disappearance) and concurrent decrease in Ig and lysozyme content of saliva [5].

Attenuation of blast reaction of lymphoid cells, participation of which is mandatory to a number of essential immunological phenomena that protect the organism against infection [6], should be interpreted as a sign of decreased immunoreactivity of cosmonauts.

Thus, it has now been demonstrated that there is a decrease in immunological reactivity of cosmonauts under the influence of diverse extreme factors of space flights,

which is manifested by a change in microbial associations of the integument, nasal cavity, mouth and throat, as well as decline of parameters of natural immunity. The set of demonstrated changes creates a danger of infectious diseases, both during and after flight.

Our objective here was to examine the correlations between microflora and preflight parameters of immunological resistance of cosmonauts who were carriers of S. aureus in the nasal cavity and subject who are not carriers of this microorganism.

Methods

The subjects were divided into two groups on the basis of being carriers of S. aureus in the nasal cavity, since expressly the anterior parts thereof are the main habitat of S. aureus.

For this purpose, we examined the quantitative characteristics of overall microflora of the upper respiratory tract referable to aerobic and anaerobic microorganisms, as well as S. epidermidis, parameters of local immunity (IgG, A and M, lysozyme) of the nasal cavity, indicators of serum immunity (complement, bactericidal activity of blood serum, IgG, A and M., phagocytic activity of leukocytes, lysozyme and specific α-antitoxic immunity according to α-antitoxin level).

The group of S. aureus carriers consisted of 21 cases (3 resident and 18 transient), and the group of noncarriers consisted of 26.

The obtained data were submitted to statistical processing. For each group of results, we calculated arithmetic means (M) and standard deviations (σ). When comparing parameters of different groups, the difference was considered significant with a reliability coefficient (P) equal to or less than 0.05-0.001. We determined the coefficient of correlation between quantity of S. aureus in the upper respiratory tract and levels of IgG, A, M in the nasal cavity and blood serum by the method of Bailey [7].

Results and Discussion

Quantitative analysis of overall aerobic and anaerobic microflora of the nasal cavity revealed that carriers of S. aureus presented a tendency toward decline in total quantity of aerobic and anaerobic microorganisms and epidermal staphylococcus, as compared to these parameters in subjects who are not S. aureus carriers (Table 1).

Table 1. Quantitative characteristics of preflight microflora of cosmonauts' nasal cavity

Group of subjects	Total amount of microorganisms		S. epidermidis
	aerobic	anaerobic	
S. aureus carriers	1.89±0.28	1.88±0.33	1.49±0.28
Noncarrier subjects	2.24±0.20	2.04±0.28	1.63±0.20

Note: Geometric means are given for number of microbial cells; in all cases $P>0.05$.

In S. aureus carriers there was reliable elevation of IgA ($P<0.05$) and IgM ($P<0.01$) levels (Table 2). It must be noted that subjects who were not S. aureus carriers

had virtually no IgM in the nasal cavity (1 out of 26 presented IgM). Lysozyme content was somewhat elevated in S. carriers.

Table 2. Parameters of preflight local immunity of cosmonauts' nasal cavity

Group of subjects	Ig, mg%			Lysozyme, μg/mℓ
	G	A	M	
S. aureus carriers	1.35±0.36	1.84±0.34	1.28±0.39	9.57±1.49
Noncarriers	0.63±0.27	0.85±0.26	0.07±0.07	6.25±1.27
P	>0.05	<0.05	<0.01	>0.05

Table 3. Preflight parameters of cosmonauts' serum immunity

Parameter	S.aureus carriers	Noncarriers
Complement (titer)	0.05±0.0091	0.055±0.0049
Blood serum bactericidal activity (titer)	96.0±20.28	90.0±24.1
Leukocyte phagocytic activity: %	38.0±2.4	37.7±2.75
index	3.76±0.39	4.3±0.61
Staphylococcal α-antitoxin, antitoxin units/mℓ	1.3±0.26	1.3±0.15
Lysozyme, μg/mℓ	2.2±0.15	1.79±0.18
Ig, mg%: G	1424.38±106.78	1193.60±55.80
A	209.80±24.28	226.96±19.30
M	171.40±12.74	137.88±9.06*

*P<0.05

Studies of serum immunity in both groups failed to demonstrate appreciable differences in parameters of cellular, humoral and specific α-antitoxic immunity. There was merely a tendency toward increased bactericidal activity of blood serum, elevation of IgG level, decrease in IgA content and phagocytic index (Wright's index) (Table 3).

We demonstrated a reliable elevation of blood serum IgM level in S. aureus carriers ($P<0.05$).

Thus, we observed activation of the system of local and serum immunity in S. aureus carriers. We demonstrated a reliable increase in IgA and IgM content of the nasal cavity in carriers, reliable decrease and virtually no IgM in noncarriers. This could be explained by the hypothesis of some authors [8, 9] that IgA and IgM may participate in binding protein A of S. aureus. Moreover, the hypothesis was expounded that a low IgA level in saliva is instrumental in adhesion of bacteria to the tonsillar mucosa and that IgA prevents penetration of bacteria through the epithelial surface of the tonsils [10].

In all probability, an S. aureus carrier state occurs as a result of change in microbial ecology of the nasal cavity, as well as decline of local immunoreactivity, which lead to "settlement" of exogenous S. aureus strains.

The results of our studies indicate that S. aureus appeared in the nose, mouth and throat after space flights (lasting 6-18 days) in cosmonauts who presented no S.

aureus in the upper respiratory tract before these flights. Evidently, this can be attributed to changes in immunological resistance, which occur under the influence of the extreme space flight factors.

Calculation of the coefficient of correlation between quantity of S. aureus in the upper respiratory tract and levels of IgG, A and M in the nasal cavity and blood serum established a mild relationship only between two parameters: quantity of S. aureus and IgM level in the nasal cavity ($r = +0.25$, $P>0.05$).

Analysis of our findings indicates that presence of S. aureus in the upper respiratory tract is associated with an increase in IgA and IgM content of the nasal cavity, elevation of IgM level in blood serum of cosmonauts, and that demonstration of IgM in the nasal cavity is unrelated to the size of the microbial focus in this biotope, since there is no reliable correlation between these two parameters.

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CORRELATION BETWEEN INDIVIDUAL DISTINCTIONS OF FUNCTIONAL ASYMMETRY OF CEREBRAL HEMISPHERES AND PILOT PERFORMANCE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 25 May 81) pp 43-45

[Article by A. A. Gyurdzhian and A. G. Fedoruk]

[English abstract from source] It has been shown that the high professional characteristics of pilots (quality of their flight performance and low susceptibility to spatial illusions) are in close correlation with the more pronounced predominance of the left hemisphere. The most informative criterion of the left hemisphere predominance that correlates with the flight performance is the index of the right ear predominance, i.e., the index of the left hemisphere predominance with respect to the speech perception. The less demonstrative parameters are the predominance of the right hand and the leading right eye.

[Text] Aviation physicians of different countries have repeatedly tried to establish a correlation between various forms of functional asymmetry of the cerebral hemispheres (CH) of pilots and their susceptibility to spatial orientation (SO) disorders, illusions of spatial position and poor achievement in flight work.

Studies were made of the significance of overt and latent left-handedness, tendency to confuse right and left sides, sequences of digits in numbers and letters in words, inability to read the mirror image of a text, construct elementary spatial conceptions, perform appropriate actions, etc. [1-4]. These features were even taken into consideration by some aviation firms in screening candidates for flight training [3].

There were several studies of the relationship between a pilot's susceptibility to spatial illusions and SO disorders, on the one hand, and asymmetry of sensitivity of the right and left vestibular systems, on the other hand [5, 6].

We have expounded the hypothesis that there is a relationship between SO and a pilot's professional skills, on the one hand, and individual distinctions of functional asymmetry of CH, on the other hand, or, in other words, individual distinctions of lateralization of CH functions [7].

Extensive material from studies of paired function of CH, motor, sensory and psychoemotional symptoms of patients with CH lesions or healthy individuals with overt

physiological dominance of one of them, which has been accumulated in the area of neurophysiology and neuropsychology [8-11], has been of appreciable assistance in conducting research in this direction.

In our previous publication [7], we reported that dominance of the left hemisphere over the right one was found more often and was more marked in a group of pilots who achieved well in learning to fly, were not involved in accidents or caused conditions for the latter to occur, than in pilots who did not achieve well in flight training, were involved in accidents and causes [conditions] thereof, as well as pilots with functional diseases of the central nervous (CNS) and cardiovascular systems.

We studied here the correlation between individual distinctions of functional asymmetry of CH and flight work achievement according to quality of performance (professional achievement) and susceptibility to spatial illusions.

Methods

We studied 654 pilots, 277 of whom were examined for quality of flight work and 377 for susceptibility to illusions of spatial position.

The pilots were divided into three groups, according to quality of flight work (professional achievement): those who had accidents and contributed to preconditions for them (83 people), those who were behind [nonachievers] in flight training (57 people) and good achievers (133).

We also formed three groups according to tendency toward spatial illusions (on the basis of questionnaire answers): those who often experienced illusions (70 people), seldom experienced them (277) and never experienced them (30).

We used the indexes of dominance of the right ear and right hand, indicators of leading role of the right eye and right leg (decussation of neural pathways in the CNS) as criteria of functional asymmetry of CH, in particular dominance of the left hemisphere.

The methods used to determine the indexes of dominance of the right ear (method of dichotic hearing) and right hand were described previously [7].

Results and Discussion

Figures 1A and 2A show the relative number of subjects with dominance of the left hemisphere (right ear, hand, eye, let) for each group of pilots, while Figures 1B and 2B show the calculated average indexes of dominance of the right ear and right leg for the relevant pilot groups.

Figures 1A and 1B illustrate functional asymmetry as a function of quality of flight work (professional achievement). It is easy to see that there is a larger number of subjects with dominance of the left hemisphere (right ear, hand, eye) and higher corresponding average index in the groups with higher flight achievements. Thus, in the group of pilots who caused accidents or conditions for flight accidents, the relative number of individuals with dominance of the right ear constituted only 26.6% (left ear dominant in 44.3% of the pilots) and averaged dominance index constituted 0.3%. In the group of poor achievers in flight training,

the right ear was dominant in 43.9% (left ear dominant in 49.9% of the pilots), with average dominance index of 13.6%. In the group of good achievers, the right ear was dominant already in 89.5% of the pilots (left dominant in only 9.7%) and averaged dominance index constituted 35.1%. Such a correlation could not be detected for dominance of the right leg.

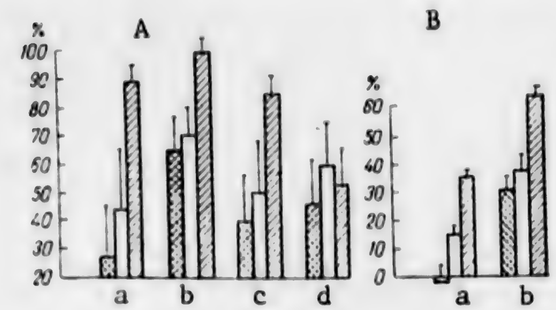

Figure 1.
Correlation between quality of flight work (professional achievement) and left hemisphere dominance. Here and in Figure 2:

A) dominance of left hemisphere
B) averaged dominance index
a-b) dominance of right ear and right hand, respectively
c-d) leading right eye and right leg
Cross-hatched columns--pilots who had accidents; white--poor achievers in flight training; striped--good achievers

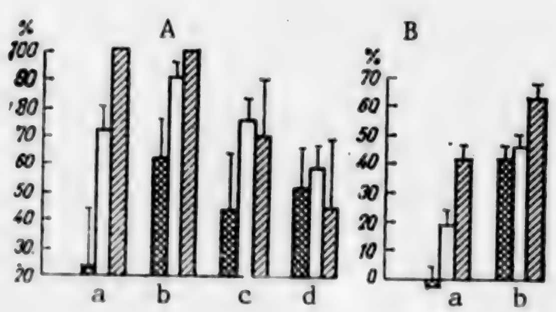

Figure 2.
Correlation between pilot susceptibility to spatial illusions and dominance of left hemisphere.
Cross-hatched columns--pilots who often experienced illusions; white--pilots who seldom had illusions; striped--never had illusions

Figure 2 illustrates the results of studying the correlation between distinctions of functional asymmetry in pilots and their susceptibility to spatial illusions in flight. The results revealed that the more marked the dominance of the right hand and particularly the right ear, the less susceptible the pilots were to inflight illusions of spatial position. Thus, among pilots who had frequent illusions the relative number of individuals with right ear dominance constituted 22.9%; among those who seldom experienced illusions this applied to 7.16% and among those not susceptible to illusions this parameter was 100%. Thus, the difference in relative number of pilots with right ear dominance in the group who caused accidents and were good achievers was almost five-fold. There was a less apparent correlation between susceptibility to spatial illusions and distinctions of assymetry for the leading eye and none demonstrable for the leading leg.

Of the 327 pilots who filled out questionnaires, 9.2% declared that they never had inflight spatial illusions, 69.4% reported that they experienced them 1-2 times (mainly illusion of rolling) and 21.4% indicated that they experienced illusions during virtually all flights under difficult meteorological conditions.

Almost all of the pilots subject to frequent illusions were in the groups of poor achievers and those who caused accidents or preconditions for them. They made errors in piloting techniques related to incorrect organization of attention, forgetting and confusing operations, incorrect estimation of distance to the ground (deck) and failure to adhere to time intervals. It was difficult for them to fly in formation; they preferred to follow a leader. When these pilots were examined in a hospital, no pathology was demonstrable, including that referable to the vestibular system.

Our findings indicate that high professional qualities (quality of flight work, minimal susceptibility to spatial illusions) were distinctly correlated to more marked dominance of the left hemisphere. The index of dominance of the right ear, i.e., the index of dominance of the left hemisphere for speech perception, was found to be the most demonstrative criterion of functional asymmetry of the CH, which correlated with flight skills.

The above-described relationship between flight performance and individual distinctions of functional asymmetry of the CH could serve as the basis for working out new methods of expert medical certification in the interests of screening and detection of the personal factor in flight accidents.

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INFLUENCE OF ORIENTATION METHOD ON QUALITY OF PILOT'S SPATIAL ORIENTATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 18 Mar 81) pp 45-49

[Article by V. V. Lapa and N. A. Lemeshchenko]

[English abstract from source] The efficiency of pilot's spatial orientation after disorientation was studied in relation to the coordinate system used, i.e., the method of orientation. It was found that the use of the egocentric system of coordinates (as compared to that of the geocentric system) caused an increase in the time of spatial perception and in the number of errors. It can therefore be concluded that the instrument-aided spatial orientation inflight (with the earth unseen) must help the pilot to develop spatial perception, reflecting spatial relations in the geocentric system of coordinates.

[Text] The problem of pilot's spatial orientation (SO) has drawn the attention of a wide circle of specialists--physiologists, psychologists, aviation physicians. Its importance is determined by the fact that flight safety depends largely on retention by the pilot of the correct idea about the position of the aircraft in relation to the ground.

Regardless of visibility of landmarks, in the opinion of a number of authors SO occurs by means of formation of a mental image of the flight, i.e., perception of the position of the aircraft in space and flying mode, which is based on experience of visual flights, theoretical knowledge and synthesis of instrument readings [1-4]. Apparently, reliability of a pilot's estimation of spatial position depends on the extent to which indicator equipment causes formation of an adequate image of the flight.

In the course of human development, there is formation of an image of space in a geocentric system of coordinates, where some element in the environment is used as the reference point for orientation [5]. In addition to the geocentric system, one can use an internal system of coordinates, when man relates objects around him to the main directions of his own body (egocentric method of orientation) [5, 6]. Most pilots fly their aircraft on the basis of the geocentric system of coordinates, i.e., they perceive their (aircraft) displacement in relation to stationary ground [1, 2, 7]. This is why some authors relate the type of indicators of the aircraft's spatial position to the image of flight formed on the basis of geocentric perception of space [7, 8, 9]. In their opinion, the better indication is offered

by using a geocentric system of coordinates, the higher the reliability of pilot's SO. However, there is still no agreement as to which mode of orientation, geocentric or egocentric, should be aided by indication of the aircraft's spatial position.

Our objective here was to assess the effectiveness and reliability of pilot's SO as a function of the orientation method used.

Methods

Methodologically, the most difficult task is to create conditions that enable the pilot to use different orientation systems with the use of the same principle of displaying information about the spatial position of the aircraft. Use by the pilot of the geocentric orientation method was obtained in flights with a laser landing system [10], in which there were three extended landmarks (laser beams) visible in space to indicate the aircraft's spatial position, one of which showed the bearing (course) of landing and the two others the specified landing trajectory (glide path). Beams projected on a plane that is perpendicular to the pilot's line of vision create a certain symbol, the shape of which unequivocally [one-to-one] shows the aircraft's position on the landing trajectory (Figure 1). The results of interrogation revealed that pilots perceived the landing symbol as being rigidly related to the ground and the aircraft as an object moving in relation to the ground; consequently, they used the geocentric system of coordinates for SO. The same principle of displaying information about the spatial position of the aircraft on the glide path for descent was applied to a flat screen installed in front of the cockpit of a flight simulator. A television image of the landing symbol was formed on the screen. It was assumed that the pilot perceived the simulator cockpit as a stationary background, in relation to which the landing symbol becomes a figure. In other words, under these conditions, it becomes possible for the pilot to use the simulator cockpit (and, consequently, himself) as the center of the orientation system, i.e., egocentric method of orientation.

In our studies, we determined the effectiveness and reliability of pilot estimation of the aircraft's spatial position following partial disorientation. The state of partial disorientation was produced by means of the following procedure: with the instrument panel and glass over the cockpit canopy covered, the instructor smoothly diverted the aircraft (trainer) from the specified trajectory. At this time, the subject removed his hands from the control stick and feet from the pedals. The following aircraft positions on the landing trajectory were simulated (see Figure 1): no deviations from landing trajector; deviation of one of the parameters--course, glide path or bank; deviations of two parameters--course and glide path, course and bank, glide path and bank; with simultaneous deviation of all three parameters--course, glide path and bank. In the first series of tests, upon uncovering the panel the subject, having assessed his spatial position, had to perform a maneuver to correct the deviations from the landing trajectory. In this series of tests, when the pilots had difficulty in assessing the spatial position using the landing symbol they could also use the flight instruments. In the second series of tests, aimed at determination of content of errors in estimating spatial position, use of instrument information was precluded: after disorientation, only the cover over the cocpit canopy glass was removed. Upon assessing the spatial position, the pilot had to report it to the instructor.

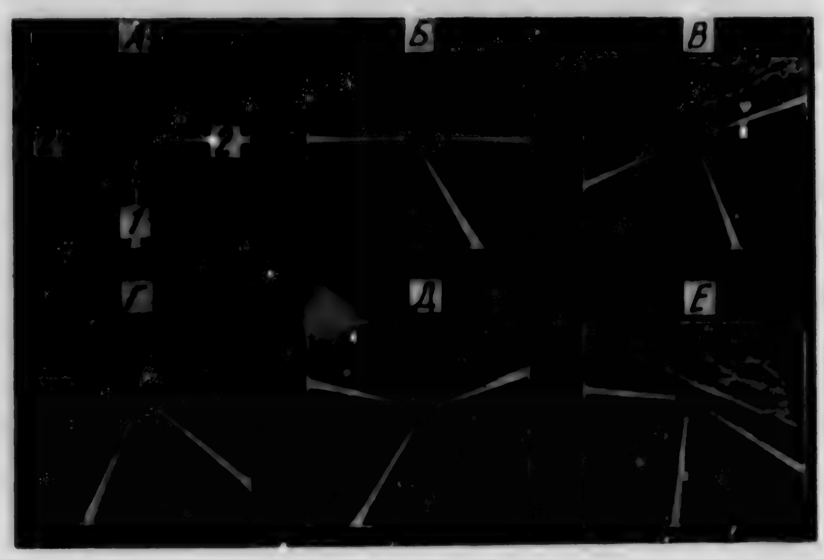

Figure 1. Appearance of landing symbol with the aircraft in different positions in relation to landing trajectory

1) course beam
2) glide path beams
А) on landing trajectory
Б) to the left of course
В) exactly on course, on the glide path, with right bank
Г) to the left of course, above glide path, with left bank
Д) to the right of course, below glide path
Е) to the left of course, above glide path, with left bank

The following were used as criteria to assess the quality and reliability of spatial orientation in the first series of tests: latency period of restoration of orientation (from the time the covers were removed to the first controlling movement); erroneous decisions in estimating the situation, motor errors; relative time of checking instruments and space ousdie the cockpit (according to cinematography of directions of vision); data from verbal report and interrogation of subjects.

In the second series of tests we analyzed (counted the number) the nature of erroneous decisions in estimating the spatial position.

The parameters of flight and pilot's actions were recorded on an oscillograph and his verbal answers on tape. All of the recordings were made synchronously by using the same time mark.

A total of 8 pilots participated in these tests: 40 landing approaches in the first series; 90 situations simulated in flight and 185 on the simulator in the second series.

Results and Discussion

First series: As can be seen in Figure 2, pilots estimated their spatial position faster during flight. The obtained differences between latency time of restoration of orientation in flight and in the simulator were not accidental. Analysis of the trajectories of eye movements revealed that in flight the pilots usually determined their spatial position by the landing symbol, without referring to instruments. After disorientation in the simulator, they referred to instruments showing the main information about the aircraft's position in space--usually the gyro-horizon and less often navigation instruments--in over 50% of the cases. Consequently, their judgment of spatial position was based on comparing information furnished by the landing symbol and instrument readings. In the course of restoration of mode (return of aircraft to landing trajectory), the relative time spent on checking instruments constituted 35-40% in the simulator and only 5% in flight. Wrong estimates of spatial position and erroneous actions were not demonstrated in flight. In the tests with the simulator, the first movements of the control stick were inadequate in 12% of the cases and resulted in even greater deviation from the landing trajectory.

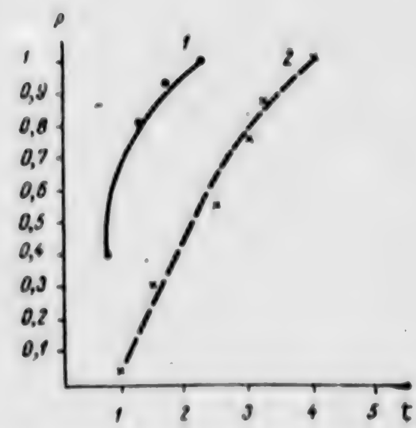

Figure 2.
Functions of distribution of latency period of restoration of spatial orientation
1) flight
2) simulator

Second series: We failed to demonstrate inflight errors in estimating spatial position, whereas their number was substantial with the simulator (21% errors). Two types of errors were observed. The first type was related to the pilot's estimation of position of guide beams forming the landing symbol in relation to the main directions of their body. The most frequent error of this type (9.8% of the cases) was wrong estimation of aircraft's position on course in the presence of banking. For example, in the situation illustrated in Figure 1B, the pilots reported that the aircraft was to the left of the landing course, orienting themselves on the deflection of the course beam from the sagittal axis of the body. In the situation illustrated in Figure 1E, the subjects could not correctly determine the deviation from course, since the direction of the course beam coincided with the direction of the body's vertical axis. In the situation shown, for example, in Figure 1Д, the pilots erroneously reported banking, which was not actually present (5.4% of the cases). The second type of error (5.8% of the cases) referred to incorrect determination of direction of deviation from landing trajectory (above--below, to the right--to the left, right bank--left bank).

The results of these studies revealed that the quality and reliability of pilot actions when using the same principle of displaying information about the spatial position of the aircraft were substantially higher in flight than the simulator. Can these differences be attributed to use of different orientation methods by the pilots? It is unquestionable that, when using the landing symbol in flight, the pilots made use of the geocent-ic system of coordinates. The validity of this

judgment ensues from the verbal account of the pilots: "I am controlling myself, the symbol, like the ground, are motionless" (pilot R.); "I am turning in relation to the ground, since I am using the landing symbol as the reference point"(pilot Z.); "I am flying the aircraft around the landing symbol, the symbol is perceived as being motionless, like the ground" (pilot S.), etc. The pilots had no difficulty in estimating the spatial position in flight, as indicated by the absence of errors.

Orientation by the landing symbol in the simulator involved certain difficulties in most pilots. The aggregate of data on both series of tests enables us to relate these difficulties to the pilots' use of the egocentric orientation method. In the first place, the pilots' statements indicate that this information model on the simulator prompts the use of the egocentric system of coordinates. In other words, the pilots perceive the landing symbol as a moving figure in relation to them: "The landing symbol is mobile on the screen, but in flight it cannot turn" (pilot A.); "I am trying to stop the symbol at a specific point on the screen" (pilot Z.), etc. In the second place, reference to instruments, usually the gyro-horizon, is an indication of difficulties in the decision making process as to spatial position. It is quite likely that the principle of indication on the gyro-horizon (movable aircraft silhouette and stationary horizon) was instrumental in forming the image of space in a geocentric system of coordinates by the pilots. Finally, the most convincing argument in favor of this hypothesis was obtained from our analysis of errors. As we have already mentioned, there was prevalence of mistakes of the first type, whose genesis is directly related to the egocentric orientation method. The genesis of errors of the second type is more complicated. They can be viewed as a manifestation of a complex process of transformation of the image of space formed in the egocentric system of coordinates (whose use is prompted by the information model) into a spatial image based on the geocentric system. The need for such transformation was attributable to the psychological set, formed in the pilots in this test, for use of the geocentric system of coordinates. In their statements, the pilots called attention to additional (as compared to flight) mental work involved in orientation using the landing symbol in the simulator: "In order to imagine that I am flying in relation to stationary beams, I had to do additional mental work" (pilot A.); "I saw that I had to not only imagine the aircraft's position in relation to the landing symbol, but the symbol's position in relation to the horizon. One does not have to do this in flight" (pilot Sh.). It is quite obvious that the algorithm of mental operations becomes more complicated because the pilot must first interpret the changed position of the landing symbol and only then determine his position in relation to the landing trajectory.

Thus, analysis of our results warrants the statement that pilot use of the egocentric system of coordinates diminishes the quality and reliability of estimation of spatial position (as compared to the geocentric orientation method). This means that to assure reliability of inflight SO, when landmarks on the ground are not visible, the indicators must assure formation of an image of spatial position that reflects the spatial relations in the geocentric system of coordinates.

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DYNAMICS OF NUTRITIONAL STATUS DURING SIMULATION OF LONG-TERM AIRCRAFT FLIGHTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Dec 82 (manuscript received 1 Apr 81) pp 49-55

[Article by I. G. Popov, A. A. Latskevich, V. Ye. Potkin, P. A. Lozinskiy, I. A. Romanova and L. I. Kolesnikova]

[English summary from source] The dynamics of the nutrient status of the test subjects who performed a simulated 22-hour flight and consumed preflight and flight diets was investigated. Subjective and objective indications (body mass changes, carbohydrate, nitrogen, amino acid, mineral and vitamin metabolism) of excessive nutrition and even acute overeating were seen. It is emphasized that, in order to prevent excessive nutrition of pilots and its harmful effects on their performance, special countermeasures need to be developed.

[Text] Proper onboard nutrition, consistent with the requirements of pilots with respect to chemical composition of food, and optimum meal schedule in the system of medical support of flight personnel is of hygienic importance, and it increases with extension of flights [1, 2].

The existing onboard diet for flights aboard aircraft lasting 4-8 h did not usually cause any worries as to sufficiency and conformity to nutrient and energy requirements of pilots. However, with increase in flight duration, a need has arisen to improve both the composition of onboard rations and schedule of consumption thereof in flight, with consideration of length of flights and specifics of the work done by flight personnel. In particular, there are data indicating that the nutrient value of the current onboard allowance for general purposes does not conform to the energy and nutrient requirements of pilots during long-term flights [2-4].

All this prompted us to conduct model experiments under ground-based conditions to make a physiological and hygienic study of the adequacy of current onboard diets to the requirements of pilots during prolonged flights.

Methods

One of the variants of scheduling meals for crews during long-term flights served as the laboratory model, with adherence to the established schedule of preflight and inflight nutrition: preflight breakfast at 0915 hours, intake of onboard

rations at 1315, 2115, 0115 and 0515 hours (i.e., every 4 hours of flight). The "flight day" lasted a total of 24 h, 2 of which were reserved for preflight preparations.

The nutritional value of the daily allowance of the subjects on the "flight" day is listed in Table 1. The data submitted warrant the conclusion that the subjects consumed with the preflight breakfast and five onboard rations more calories and essential nutrients per day than they could have had by consuming the entire ground-based flight ration on preflight training days. The current ground-based flight ration, with the supplement for jet aircraft, contains an average of 4890 kcal, 140 g protein 173 g fat and 660 g carbohydrate [1, 2, 5]. If we compare the nutrient value of the daily allownace of the subjects on the "flight day" to physiological nutritional standards, we shall find that their allowance exceeds the daily requirements of energy, protein, fat and carbohydrates that are recommended for the adult able-bodied population [6]. Thus, the current daily food allowance for pilots during long-term flights with the use of standard onboard rations is sufficient for both light and heavy physical work.

Table 1. Nutritional value of daily food allowance of subjects in a simulated long-term flight

Parameter of nutritional value	Preflight break-fast	Onboard meals (5)	Total in daily ration
Energy value, kcal	1211	5025	6236
Protein, g	38,5	141,51	180,01
Fat, g	64,6	136,39	200,99
Carbohydrate, g	99,52	853,22	952,74
Potassium content, mg	622,7	4021,9	4644,6
Phosphorus content, mg	334,1	1779,0	2113,1
Calcium content, mg	595,8	358,3	954,1
Sodium content, mg	1445,0	5729,8	7174,8

Two series of experiments were conducted on the same three subjects. The difference between the series consisted of the fact that Hexavit, a multiple vitamin product, was used as a supplement in the second series. In the first series, vitamins were furnished in the foods and chewable vitamins provided in the onboard rations. During the period of "preflight" training [preparations], the subjects ate three times a day, with intake of as much of the flight ration as they needed. Their actual food intake consisted of an average of 3886 kcal, 117.7 g protein, 181.9 g fat and 417.3 g carbohydrate per day. During the "flight" the onboard rations had to be consumed entirely.

During the "flight days" the estimated expenditure of energy by the subjects should have constituted about 3000 kcal/day for individuals weighing 70 kg. Considering the individual body weight, energy expenditure per day should have been somewhat higher: 3900 kcal for subject L., 3557 kcal for subject K. and 3383 kcal for subject B.

Information in the literature warrants the conclusion that the estimated expenditure of energy by the subjects was close to the energy expended by flight crews during long-term flights. Thus, I. M. Buznik writes that, according to the statements of many authors, pilots expend 3000-3500 kcal per day. In 1971, he arrived at the conclusion that the crews of aircraft making prolonged flights seldom expend more than 3000 kcal/day [7]. On the basis of studies pursued in the United States, it can be concluded that energy expended by pilots during horizontal flights constitutes an average of 94.92 kcal/h/70 kg body weight. This amount of energy expenditure corresponds to light and very light work [3, 8]. Consequently, energy expenditure should constitute about 2100 kcal during the 22 h of flight simulated in our experiments. For this reason, considering preflight work and additional activity in flight, energy expenditure should not exceed 3000 kcal/day for individuals weighing 70 kg. According to Farmer's data, daily energy expenditure by pilots constitutes only 2500 kcal [9]. Thus, the energy expended by our subjects was quite comparable, on the whole, to actual expenditure of energy by flight personnel during prolonged flights.

The subjects kept a diary during our studies. They were regularly questioned about their general well-being, appetite, subjective sensations referable to the gastrointestinal tract, sufficiency or excessiveness of food.

Results and Discussion

In the first series of tests, the appetite of all subjects remained good during the preflight breakfast and first onboard ration intake. By the time the second ration was consumed, this parameter was diminished in one case and remained good in the other two. By the time of the third onboard meal, two subjects had less appetite, but it remained good in the third. By the time of the fourth meal, the appetite of the same two subjects diminished even more, but remained satisfactory in the other one. At the time of the fifth onboard meal, all three subjects lost their appetite. Starting with the third onboard meal, two of them reported a general excessiveness of food and they had progressive feelings of a full stomach and intestine. On the whole, the same findings were made in the second series of studies. The progressive sensation of full "stomach" was associated with constant general discomfort, appearance of meteorism, perspiration and other autonomic reactions. Of course, the general discomfort also increased as a result of increasing fatigue during the second half of the "flight," restricted movement, monotonous static exertion in seated position, disruption of usual pace of life, sleep deprivation, etc. Thus, starting with the third onboard meal or fourth food intake of the day, two out of the three subjects reported that there was excessive food and overt signs of overeating.

Table 2 lists data on changes in the subjects' weight, as well as weight of foods in the daily ration and fluid intake. According to Table 2, all subjects gained weight during the "flight day." After a bowel movement upon the end of the day-long experiment, their weight dropped by 0.3-0.4 kg, but remained higher than before the flight. During the "flight" only relief tubes [urinals] were available to the subjects (as in many aircraft). In the second series of studies, there was relatively less weight gain due to higher renal output. The change in weight of the subjects was correlated to some extent with the amount of fluid intake, which was not limited. Interestingly enough, the subjects' weight did not drop to the base level in the week-long interval between the first and second "flights."

There was little change in their weight on days preceding the study. Thus, the subjects' weight was consistent with their subjective quantitative assessment of nutrition on the "flight" day and confirms the fact that with intake of food 6 times a day (preflight breakfast and 5 onboard meals) in the amounts established for preflight and onboard diets distinct signs of acute overeating can develop. Some individuals may develop gastrointestinal discomfort and diminished appetite at later stages of flight and these signs may be less marked, as we noted above for one of our subjects.

We examined carbohydrate, nitrogen, amino acid, mineral and vitamin metabolism in order to assess the dynamics of biochemical parameters of nutritional status of the subjects.

Table 2. Changes in subjects' weight, as well as weight of foods and fluid in 24-h ration for "flight day"

Series	Subjects	Body wt., kg			total wt. of foods including juices, kg	water content in ration, including juice, kg	total fluid (tea, coffee, water) intake on "flight day," kg
		Morning, fasting	24 h after "landing"	change			
1	L.	91,5	94,8	+3,3	3,082	1,455	2,4
	K.	83,1	85,3	+2,2			1,7
	B.	79,0	81,6	+2,6			1,6
2	L.	93,3	95,4	+2,1	3,082	1,455	1,9
	K.	84,2	85,8	+1,6			1,4
	B.	80,0	81,6	+1,6			1,2

Some interesting findings were made with respect to blood glucose content. This parameter was assayed by the orthotoluidine method, in which a concentration of 60-100 mg% is considered the physiological norm. Blood samples were taken from a finger before each meal, then 30, 60 and 90 min after meals. A sugar loading test was performed before our experiment, in which the sugar curves were found to be in the physiological range.

In the first series of studies, all subjects presented normal (closer to the bottom range of normal) blood glucose content prior to intake of the first onboard meal. Glucose content constituted 106 mg%, i.e., somewhat above normal, in only one of them (subject B.) before intake of the second onboard allowance, and it was 115 mg% in the 60th min after food intake. Before taking the third onboard meal, blood glucose concentration was in the normal range in all subjects, but closer to the tope of the range. By the 60th min, there was a drop of glucose level to the top normal range in only one subject, and it remained elevated in the others (106-152 mg%). Before intake of the fourth meal, blood glucose concentration was above normal in all subjects (104-115 mg%), and it remained high in the 90th min after the meal (115-144 mg%). Before intake of the fifth onboard meal, glucose content was 106 mg% in one subject and near the top of the normal range in the

others. This parameter remained high--105-120 mg%--in 2 of the subjects after 60 min, and even in the 90th min constituted 110 mg%. Consequently, with increase in duration of the "flight" and intake of successive onboard meals we observed a general elevation of blood glucose level, which exceeded the physiological norm. There was slow normalization of blood glucose concentration after intake of food. The greatest changes in blood glucose content were noted during the second half of the "flight," which coincided with intake of the 3d (2130 hours) and 4th (0130 hours) meals. In general, analogous findings were made in the second series of studies. The most probable cause of such dynamics of blood glucose concentration is apparently the progressive food excess against the background of hypokinesia in seated position, minimal expenditure of energy, developing general fatigue and increased intake of readily assimilable carbohydrates.

Total nitrogen excretion in urine during the "flight day" constituted 15.2±1.14 g. It is generally believed that with normal protein metabolism 14-20 g total nitrogen is eliminated in 24-h urine [10, 11]. Excretion of total nitrogen depends on the protein intake and state of nitrogen balance. It is also related, to some extent, to muscular mass of the body [7]. The above-cited total nitrogen excretion corresponds to 109.31 g food protein (amount of protein equals amount of total nitrogen in grams multiplied by the factor 6.25, with subsequent increase of the obtained figure by 15% to take into consideration total extrarenal elimination). The estimated value thus obtained is substantially lower than the actual amount of protein consumed by the subjects on the "flight" day in their daily ration--180 g/day. On the days preceding the flight experiment, total nitrogen excretion constituted 14.52±1.22 g/day which, according to analogous calculations, corresponds to 104.36 g food protein. The subjects took in about 111.7 g protein per day on "preflight" days. According to confidence intervals ($M \pm m \cdot t_{95}$), total nitrogen excretion constituted 12.28-18.14 g on the "flight day" and 11.38-17.66 g on "preflight" days. The differences in nitrogen excretion with intake of the flight diet and onboard meals were unreliable. This automatically raises the question of diminished assimilation of food protein on the "flight day," for example, due to excessive food intake and poorer digestion thereof, as well as absorption of nitrogen-containing substances. In order to answer this question, it is expedient to compare excretion of total nitrogen in urine and amount of nitrogen in daily food intake before and during the "flight." According to the data of D. H. Calloway [D. Kh. Kellovey], in the case of a casein diet, about 90% of the nitrogen ingested by man is excreted in urine [12]. V. G. Vysotskiy believes that on an ordinary diet about 85% of taken nitrogen is excreted in urine and, along with a few others, this figure confirms best to virtually normal protein intake [13]. Excretion of total nitrogen in urine on preflight training days, when the subjects were on the flight rations and ate as their appetite dictated, constituted 81.25% of total nitrogen contained in consumed food. On "flight days," this correlation was lower and constituted about 52.81%. There was less protein of plant origin in the onbaord rations than preflight ones. All this warrants the conclusion that there was diminished assimilation of food protein on the "flight day." This is attributable primarily to the excessive intake of food, worsening of processes of digestion and assimilation of food protein.

We assayed blood plasma levels of 17 free amino acids in order to examine the dynamics of amino acid metabolism of fasting subjects before and after the "flight day." This was done using an automatic analyzer. All subjects presented elevation of all amino acid levels, with the exception of cystine, by the end of the

Table 3. Vitamin C_1, B_1, B_2 and B_6 excretion in urine on preflight trainings days and during simulated long-term flights

Series of studies	24-h vitamin excretion in urine, mg							
	ascorbic acid (C)		thiamin (B_1)		riboflavin (B_2)		4-pyridoxic acid (B_6)	
	"preflight" days	"flight" day	"preflight" days	"flight" day	"preflight" days	"flight" day	"preflight" days	"flight" day
I	15.49±3.5	21.71±1.7	0.153±0.04	0.39±0.01	0.26±0.08	0.57±0.06	2.93±0.73	3.36±0.62
II	23.94±5.7	32.38±1.9	0.3±0.07	0.46±0.04	0.3±0.07	0.46±0.04	2.96±0.04	5.14±0.68
Excretion with normal vitamin supply (according to V.V. Yefremov)	20—25		0.15—0.5		0.3—1.0		1.5—2.5	

"flight day." This increase was reliable for glycine (from 1.29±0.03 to 1.51±0.03 mg%) and leucine (from 1.40±0.05 to 1.56±0.02 mg%, $P<0.05$). Cystine content dropped from 0.78±0.01 to 0.75±0.02 mg%. This tendency toward decrease in cystine concentration could be attributed to decreased intake with food of both cystine and methionine, due to use of canned meat in the onboard diet, which is limited in both these amino acids. Total amino acids, as well as the sum of essential and unessential amino acids increased reliably by an average of 10% ($P<0.01$). Total amino acids increased from 25.7±0.28 to 28.08±0.22 mg%, total essential amino acids from 10.73±0.11 to 11.52±0.07 mg% and nonessential from 14.97±0.14 to 16.56±0.21 mg%, which is indicative of high overall supply of these amino acids in the body. There was negligible change in correlation between essential and unessential amino acids, from 0.72±0.01 to 0.69±0.01. Such a change is indicative of a tendency toward relatively faster increase in levels of unessential amino acids in plasma, which is usually considered to be less favorable than an increase in ratio of essential to unessential amino acids at the expense of the former. Evidently, these changes in free amino acid content of blood plasma are due primarily to the substantial increase in amino acid intake with food, which was observed by a number of authors in the case of a high protein diet [14]. The tendency toward greater relative increase in unessential amino acids may be indicative of poorer assimilation of essential amino acids and some impairment of amino acid balance in food.

Daily excretion of macroelements in urine constituted 160±23 meq sodium, 68±10 meq potassium, 286±58 meq calcium, 1658±96 meq phosphorus and 210±22 meq chlorides. According to these data, elimination of macroelements in urine during the "flight day" on the onboard diet was in the range of average physiological norms. This means that the amount of macroelements in the daily diet of the subjects was sufficient or even somewhat more than the accepted physiological nutritional standards [15]. Thus, we should consider that the body was adequately provided with macroelements by the onboard diet.

Table 3 lists the results of assaying daily excretion in urine of vitamins C_1, B_1, B_2 and B_6 on "flight days" on the onboard diet and on "preflight" training days on flight rations.

In analyzing the data in Table 3, it must be borne in mind that the subjects received vitamins only in food in the first series of studies, including the "flight day," in the form of chewable [caramel] vitamins provided in the onboard allowance. In the second series, they were given additionally one Hexavit tablet on "preflight" training days and two on the "flight day": with the preflight breakfast and third meal onboard.

Vitamin supply of subjects, with reference to vitamins C and B_2 was below the physiological norm, while that of B_1 and B_6 was rather high, according to excretion in urine, on "preflight" preparation days without additional vitamin supplements. On the first "flight day," there was an increase in excretion of all vitamins, and it reached levels indicative of good supply thereof to the body.

In the second series of studies, there was an increase in supply of all vitamins because of Hexavit intake, as compared to the first series, and it was in the physiological range. Thus, intake of two Hexavit tablets on the "flight day" increased even more intake of these vitamins, while 24-h excretion thereof was indicative of rather high functional supply of vitamins C, B_1, B_2 and B_6. Excretion of ascorbic acid and pyridoxine even exceeded the physiological norm.

Consequently, inclusion in the onboard allowance of a chewable vitamin and issuing Hexavit once in flight constitute a rather effective means of increasing the body's supply of vitamins C, B_1, B_2 and B_6 when using onboard rations for long-term nutrition, including canned goods.

Thus, the existing system of onboard nutrition, by virtue of the high nutritional value of onboard rations and preflight breakfast (lunch, supper) provided on the ground, furnishes pilots with sufficient amounts of the main nutrients and energy during long-term flights to compensate for the most varied metabolic expenditures, including moderate and heavy work. Such a system of onboard nutrition is a reliable material base for organizing optimum nutrition during long-term flights and preserving a high degree of fitness in flight personnel. At the same time, complete intake of the existing onboard meals every 4 h when there is drastic restriction of muscular activity and energy expenditure as a whole could lead (at least in some crew members) to eating to excess and, consequently, development of signs of acute overeating. Excessive intake of food has an adverse effect on general well-being; it elicits discomfort referable to the gastrointestinal tract, depresses the appetite, increases boredom about foods and is instrumental in general fatigue and drowsiness. Some individuals may present prolonged elevation of blood sugar (to levels exceeding the norm), particularly during the second half of a flight and at night. There is poorer assimilation of the most valuable part of the diet--protein.

It is necessary to improve the diet in order to prevent development of overeating in pilots during long-term flights. First of all, attention must be given to the mealtime schedule and composition of onboard rations for flights lasting over 8-12 h. It is imperative to instruct flight personnel appropriately in the course of medical monitoring of onboard food intake during prolonged flights.

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SOME FEATURES OF EVALUATION OF WORK CAPACITY AND FATIGUE IN HELICOPTER PILOTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 22 Dec 80) pp 55-58

[Article by Yu. N. Kamenskiy]

[English abstract from source] In helicopter pilots the direct index of their work capacity increased while indirect indices decreased in the course of the flying shift. The peak of their professional performance occurred at the end of the flying shift coinciding with the expressed feeling of fatigue. Evaluation of professional work capacity using direct methods does not yield adequate information about the state of pilots, making them unsuitable to diagnose fatigue and to measure permissible work load. Proper diagnostics of fatigue does not necessarily require examinations of the pilot's state inflight. Adequate information can be obtained on the ground during the flying shift.

[Text] Questions of evaluating work capacity and identifying pilot fatigue have and remain among the main problems of physiology of flight work. In each specific instance, these problems are solved on an individual basis, but with consideration of general methodical and methodological principles. While the latter have already been sufficiently worked out [1-4], things are not yet entirely clear concerning the former--procedures for assessing pilot fatigue and work capacity.

It is a complex task to assess the professional work capacity of an operator. As it applies to pilots, this complexity increases due to one of the distinctive features of the flying profession--the need to uneventfully complete a flight, no matter what difficulties or changes in the pilot's functional state arise. For this reason alone, the concept of pilot "work capacity" acquires a vague content, and it becomes rather problematic to assess it on the basis of piloting quality.

Since fatigue is a decline of work capacity caused by work, psychophysiological evaluation thereof can be reduced, to some extent, to a description of fatigue. However, if fatigue is not associated with a decline of work capacity, such interpretation may be questionable, from the standpoint of practical determination of fatigue.

Our objective here was to determine the correlation between changes in the direct index of helicopter pilot work capacity and indicators of certain professionally important psychophysiological traits characterizing the state of fatigue.

Methods

We examined 112 helicopter pilots who performed ordinary commercial flights. They were examined before, during and after flights. The level of professional work capacity was determined by the indicators of variability of rotor revolutions during descents and landings [5]. The revolutions were recorded every 5 s, and then we calculated the coefficient of variation (CV). An indirect evaluation was made of pilot work capacity in flight on the basis of the results of testing reaction time (RT) according to N. I. Frolov [6].

We determined the reaction to a moving object (RMO), which is considered of professional importance to helicopter pilots, 40-60 min before and 40-60 min after flights.

We studied the pilots' evaluation of their state by means of anonymous questionnaires. The results were submitted to statistical processing, under conditions of 90% probability of mean values and 95% reliability of differences therein.

Results and Discussion

There was an increase in variability of rotor revolutions during the first 2-3 flights at the descent and landing stages (Figure 1). Thereafter, the CF decreased, reaching reliably lower levels in the 7th-8th flights than the first.

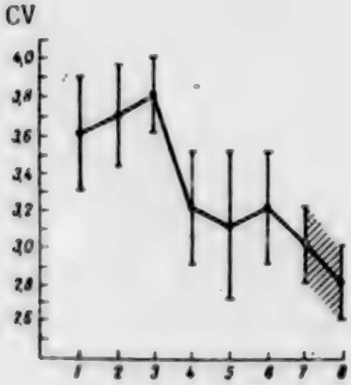

Figure 1.
Change in variability of rotor revolutions in the course of the flight shift.

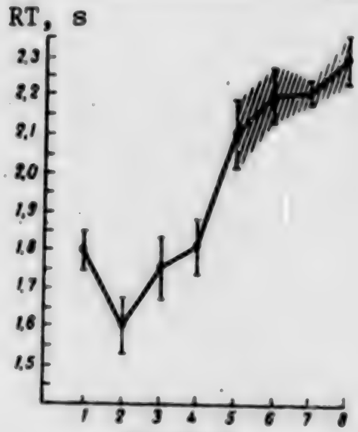

Figure 2.
Changes in reaction time in the course of flights

In Figures 1, 2 and 3, the crosshatched sections refer to reliable changes.

There was a tendency toward decline of RT at the start of the flight shift (Figure 2), followed by a rise, reaching initial values in the 4th flight and increasing drastically in the 5th, i.e., the dynamics of RT were the opposite of CV dynamics in the course of the flying shift: improvement of indirect indicator of work capacity during the first flights was concurrent with some worsening of flying skills. There was a change in this correlation during the last flights.

It is important to note that, even with simulation of flying, there was improvement of professional skills after "flights," in spite of pilot fatigue [7]. This phenomenon is based on the distinctions of central nervous system function in the presence of marked fatigue. Probably, in this case there is development of a unique state of higher nervous activity, which is associated with improved function of complex neuroreflex structures that provide for execution of professional skills. Apparently, it is for expressly this reason that the direct indicators of operator work capacity can improve in the presence of fatigue. However, there is temporary worsening of its indirect indicators. This phenomenon has been described as the phenomenon of "minimization" of functions that are not of decisive significance to performance of professional duties. Evidently, in our case, the complex visual-motor reflex, on which is based the method of determining RT, is referable to such functions. In view of the discrepancy between direct and indirect indicators of fatigue, the degree thereof should be assessed primarily from the standpoint of providing for safe flights. However, a certain contradiction then arises.

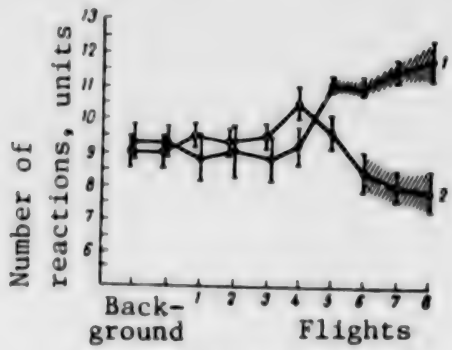

Figure 3.
Change in number of delayed (1) and premature (2) RMO in the course of flying shift

If the functional state of the pilot is evaluated according to quality of flight performance, fatigue can be considered an acceptable phenomenon, since piloting quality not only fails to be affected by it, it even improves. However, there is always a possibility in flight of unexpected situations that may lead to an accident in the presence of pilot fatigue [8]. For this reason there is full justification for the requirement of assuring a high level of flight safety by preventing pilot fatigue at the end of his work shift [9].

This requirement is not met if the functional state of the pilot is evaluated according to flying quality. At the same time, pilots present marked fatigue at the end of their flying shifts. This is indicated, in this instance, by the change in components of RMO, which reflects the correlation between the main nervous processes in the cerebral cortex (Figure 3).

The increase in number of premature reactions after the 4th flight is an indication of beginning fatigue [10]. Disinhibition of the excitatory process coincided with appearance of a tired feeling in some (15.3%) pilots. However, improvement of professional work capacity began concurrently with this (see Figure 1).

A decrease in number of premature reactions and increase in delayed reactions (see Figure 3) are typical of marked fatigue [10]. One should have also expected impairment of work skills. However, in our case, flying skill, on the contrary, improved, in spite of the fact that fatigue had reached a significant degree. The latter is confirmed by the increasing feeling of fatigue, according to the questionnaire data: in 42.8, 86.7, 85.7 and 92.3% of the pilots after the 5th to 8th flights, respectively, as well as increase in number of cases of negative attitude about continuing the flights: in 35.7, 66.7, 78.6 and 96.2% of the pilots after the 5th-8th flights, respectively. The above times of appearance and increase in fatigue of helicopter pilots conform to data of other authors [11, 12].

Can one discuss diminished pilot work capacity if piloting quality improves? Probably one can, if work capacity is construed as the potential psychophysiological reserves of the body [13]. However, the very word, "work capacity," is usually associated with its direct indicators, which makes it more difficult to use this concept for indirect indicators.

The above-mentioned correlations between direct and indirect work capacity parameters are indicative of the following.

In the first place, evaluation of flying performance does not provide adequate information about the functional state of a pilot's organism. Moreover, such evaluation obscures the true state of affairs, and it cannot be considered acceptable for diagnosing pilot fatigue and making a decision as to the admissibility of a given flight work load.

In the second place, apparently it is not mandatory to examine the inflight functional state of pilots to determine the presence of fatigue. Dynamic examination of pilots on the ground during the flight shift provides a sufficient and reliable volume of information in this regard, provided the appropriate methodological procedures are used [4].

In the third place, it is imperative to improve work schedule organization for helicopter crews on the basis of dynamic study of pilot fatigue in the course of their work shift.

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PHYSIOLOGICAL AND HYGIENIC RATING OF TRANSPORT HELICOPTER VIBRATION DAMPER

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 16 Apr 81) pp 58-61

[Article by Yu. G. Matveyev and Yu. N. Kamenskiy]

[English abstract from source] The vibration damper reduces vibrations in the helicopter cockpit 2-3-fold during horizontal flight and 4-5-fold at the braking stage. The use of the vibration damper helps better reception of the panel information and helicopter control, improves the working conditions and maintains the high performance of the crewmembers during the flying shift.

[Text] Vibration is one of the main deleterious factors in the cockpits of helicopter crews [1-3]. Exposure to it during the flight shift alters the functional state of pilots and causes premature fatigue [4]. This is associated with diminished reliability of piloting and development of preconditions for flight accidents, particularly during landings [5].

For this reason, helicopters are equipped with vibration-damping devices, in particular, dampers of the pendulum type, at the stage of design and completion of new helicopters, along with development of the means of reducing vibration of the craft. Our objective here was to examine and offer a physiological rating of the efficacy of such a damper, when installed on a medium cargo helicopter.

Methods

Vibration was measured on 2 helicopters in the course of 69 commercial flights, before and after installing dampers. This volume of measurements provided a representative sample of flying conditions (take-off and landing mass, centering, duration of flight). The readings were taken on the floor of the cockpit and pilot's seat in accordance with GOST 23719-79 in three mutually perpendicular directions: "feet-head" vertical (Z axis), "back-chest" horizontal (X axis) and "side-side" horizontal (Y axis). We used a set of miniaturized vibration-measuring equipment.

In processing the tape recordings, we determined the logarithmic levels of mean-square values of rate of vibration in the range of octave bands, with geometric mean frequencies of 2 to 250 Hz. We performed narrow-band analysis to determine the structure of the vibration signal. The parameters of vibration were recorded at all stages of flight: during take-off, climb, in horizontal flight, descent and

landing. The averaging time for the established flying modes constituted 32 s and for transient modes it was 8 s.

We examined 320 crew members, who had flown aboard helicopters with (main series of studies; 160 people) and without (control, 160 people) vibration dampers, before and after flights. The pilots were examined 60-90 min before the start of their work shift and 40-60 min after its end. All of the pilots in both series of studies were divided into 8 groups of 20 in each, according to their flight load (from 2 to 9 h per day).

We used professionally important psychophysiological parameters in our examination: critical fusion frequency (CFF), reaction to moving object (RMO), precision of movement coordination (PMC), reproduction of muscular exertion (RME). The RMO data were expressed as the ratio of number of premature reactions (RMO_p) to number of delayed reactions (RMO_d), which was arbitrary called the indicator of nervous processes (INP).

The circulatory system was evaluated on the basis of the results of measuring pulse rate (PR), systolic and diastolic arterial pressure (AP_s and AP_d), and the system of external respiration according to parameters of functional reserves--maximum ventilation (MV) and pneumotonometry (PTM) according to Kh. A. Izakson [6].

The parameters of vibration were submitted to statistical processing with confidence probability of 90%. The results of psychophysiological tests were processed statistically with 95% probability of differences in mean values.

Results and Discussion

It is expedient to describe the numerous vibration states of a helicopter in two stages to assess the efficacy of dampers: horizontal cruising (maximum duration) and braking (maximum level of vibration). It has been established that the spectrum of vibration of a medium cargo helicopter is determined by the component corresponding to the fifth harmonic of rotation of the rotor, which is in the 16 Hz octave and presents maximum levels in the vertical direction. The mean vibration rate in the 16 Hz octave in helicopters that are not equipped with vibration dampers reached 111-112 dB on the floor and chair seat in horizontal flight and 117 dB during braking. Use of the damper reduced vertical vibration at the horizontal stage of flight by 2-3 times (Figure 1) and during deceleration by 4-5 times (Figure 1).

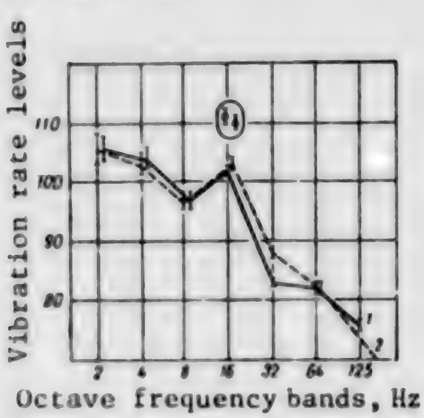

Figure 1.
Spectra of levels of vibration rate at the pilot's work place in a helicopter equipped with vibration damper, measured in horizontal flight.
In the oval--rate of vibration of floor (circle) and seat (triangle) of helicopter without vibration damper. Vertical lines--90% confidence interval of mean level of vibration rate

1) floor 2) seat

Table 1. Dynamics of psychophysiological parameters of pilots in main and control study series in the course of flying shift

Time of examination	CFF, Hz		RME, arbitrary units		PMC, arbitrary units		INP, arbitrary units	
	O	K	O	K	O	K	O	K
Preflight	38,2±0,2	38,0±0,3	4,9±0,2	5,2±0,2	5,1±0,3	4.8±0,2	0,92±0,05	0,84±0.04
After flights lasting:								
2 h	39,5±0,3	38,6±0,3	6,6±0,3	6,8±0,4	5.2±0,4	4,5±0,1	1,54±0.10	1.87±0.12
3 "	39,4±0,2	37,8±0,3	6,2±0,1	6,4±0,5	4.9±0,3	4.2±0.1	1,27±0,08	1.12±0.03
4 "	38,7±0,3	38,7±0,4	6,3±0,2	5,7±0,3	4.7±0,3	3.8±0.2	1,04±0,09	1,03±0.11
5 "	38,2±0,3	36,1±0,4	5,9±0,2	3,0±0.5	4,6±0,4	2,0±0,1	0,86±0.12	0.72±0.12
6 "	37,3±0,4	36,0±0,4	5,7±0,3	3,1±0,2	3,8±0,4	2,2±0,31	0.82±0,11	0,68±0,10
7 "	36,8±0,4	36,3±0.4	5,1±0,3	2,8±0,3	3,5±0,3	2,3±0,2	0,78±0,10	0,65±0,13
8 "	36,1±0,5	36,1±0,5	4.6±0,4	2,6±0,4	3,3±0.3	2,1±0,2	0,75±0.13	0,66±0.12
9 "	36,2±0.4	35,8±0,5	3,8±0,3	2,7±0,3	3.1±0,4	1,9±0,1	0,71±0,12	0,71±0,10

Key--here and in Table 2: 0) main series K) control

Table 2. Dynamics of autonomic parameters of pilots in main and control study series in the course of flying shift

Time of examination	PR/min		AP_s, mm Hg		AP_d, mm Hg		PTM, mm Hg		MV, ℓ/min	
	O	K	O	K	O	K	O	K	O	K
Preflight	74±1,2	72±1,0	120±1,8	119±1,5	80±2,0	76±1,5	125±3,0	122±2,0	131±2,1	126±1,3
After flights lasting:										
2 h	80±1,8	80±1,4	126±2,0	128±1,8	84±2,1	88±2,4	124±4,0	120±3,0	133±4,1	130±3,2
3 "	80±1,6	78±1,6	126±2,1	126±1,9	85±2,1	86±2,1	123±2,0	124±2,0	130±3,2	128±2,1
4 "	78±1,7	80±1,5	128±1,8	130±1,7	84±1,9	86±1,8	124±3,0	120±2,0	132±3,1	126±2,4
5 "	78±1,8	78±1,8	127±1,9	129±2,0	83±1,8	84±2,0	120±2,0	114±3,0	128±2,2	120±3,1
6 "	76±2,0	78±2,0	126±1,8	128±2,1	81±2,1	84±2,1	117±3,0	110±4,0	124±3,1	117±3,3
7 "	76±2,1	74±1,9	125±2,1	130±2,0	80±2,2	80±2,0	112±3,0	112±3,0	118±4,2	118±2,3
8 "	74±1,9	76±2,1	126±2,1	129±2,2	82±2,1	82±2,4	112±4,0	108±2,0	113±4,1	116±4,2
9 "	74±2,2	74±2,0	128±2,0	128±2,1	81±2,3	80±2,3	108±5,0	102±3.0	110±5,2	115±3,4

According to the pilots' statements, working conditions aboard helicopters equipped with vibration dampers are significantly improved, it is easier to read instruments and fly the craft, particularly at deceleration and landing stages. All of the pilots observed that much less fatigue is experienced after flights.

Objective data were also indicative of better functional state of pilots in the main series, as compared to the control. The psychophysiological parameters presented phasic dynamics in both series in the course of the work shift. There were substantial quantitative differences between values obtained in the two series. Thus, after flying for 2 h there was more appreciable improvement of parameters in the main series than the control: CFF increased by 3.4 and 1.5%, accuracy of RME improved by 35 and 31%; INP rose by 67 and 123%, respectively (Table 1). The latter indicates that there was less impairment of correlation between the main nervous processes in pilots of the main series.

After a flight of 3-4 h, there was relative stabilization of parameters in the main series, whereas in the control they all declined, but remained above the base level. These changes are indicative of early signs of fatigue. A substantial worsening of psychophysiological parameters was noted in pilots of the control series after flying for 5 h: CFF decreased by 5%, accuracy of RME by 44%, PMC by 50% and INP by 2.4%. These changes can be qualified as evidence of marked pilot fatigue [7, 8]. Subsequently, all of the parameters stayed close to this level to the end of the flying shift (see Table 1).

In the main series, a marked decline of parameters was noted only after flying for 7 h, i.e., 2 h later than in the control. Thereafter, the parameters became stabilized, but remained at a higher level than in the control series (see Table 1).

In the control, the circulatory parameters first (up to 5-6 h flying time) increased and held at a high level (Table 2), after which PR started to decline and come close to the base level; AP_s remained high to the end of the flying shift and AP_d dropped. There was virtually no change in parameters of functional reserve of external respiration at the start of the shift. After flying for 5 h PTM parameter reliably decreased by 6.6% and subsequently presented a distinct tendency toward decline. MV decreased by 7.2% after flying for 6 h, and this tendency also persisted to the end of the shift.

The dynamics of circulatory and respiratory parameters were analogous in pilots of the main series, but the changes were not as significant (Table 2).

On the whole, the changes in psychophysiological and autonomic parameters of pilots in both series were indicative of the fact that their functional state underwent several phases during the flight shift. The time of development and intensity of these phases varied in different series. Since working conditions in both series differed virtually solely in vibration levels, it is justified to attribute the differences in functional state of pilots to different levels of this factor.

There was more appreciable change in functional state of pilots exposed to vibration with intensity of 112 dB than 105 dB. A phase of marked fatigue developed after 5 h of flying at 112 dB and after 7 h at 106 dB vibration. Moderate changes in psychophysiological parameters were indicative of the fact that the body retains some reserves even after flying for 8-9 h.

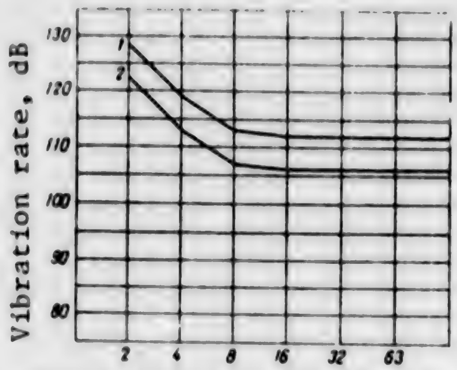

Figure 2.
Recommended permissible levels of vibration in helicopter cockpits
1) 5-6 h exposure 2) 8-9 h exposure

Our data enable us to construct the spectra of permissible levels of vibration with exposure for 5-6 and 8-9 h. If a frequency of 16 Hz were to taken as the base level, the spectrum of permissible levels would pass through the 112 dB point, according to GOST 12.1.012-78, for 5-6 h and 106 dB point for 8-9 h (Figure 2).

Thus, the vibration damper lowered the level of vibration at the pilot's work place by 2-3 times in cruising mode and by 4-5 times at the stage of deceleration. With a lower vibration level, working conditions are better, it is easier to read instruments and control the helicopter, and the functional state of pilots remains high during the flight shift; consequently, there is more effective use of helicopters in the national economy.

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SIGNIFICANCE OF BONE DENSITY TO SPINAL TRAUMA RELATED TO PILOT EJECTION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 2 Feb 81) pp 62-63

[Article by A. P. Kozlovskiy, G. P. Stupakov, V. P. Dryannykh, A. B. Arsent'yev and V. V. Chuntul]

[English abstract from source] The examinations of 27 pilots, 10 of which were catapulted, demonstrated that fractures of the spinal column occurred in those pilots (5 cases) whose heel bone density (as measured by the method of direct photon absorption) was lower than in the controls (17 cases) and in those pilots who did not have traumas, when being ejected.

[Text] Analysis of ejection-related traumatism performed by foreign authors revealed that a significant part thereof (9 to 43%) is referable to vertebral fractures [1]. The features of the ejection seat and belt system [2], as well as failure to maintain the proper position [3], are mentioned as factors causing them to occur under the influence of ejection-related accelerations. However, these factors should be viewed merely as contributory to increased flexure of the spine and marginal strain on vertebral bodies, lowering resistance to impact accelerations. On the whole, however, a vertebral fracture occurs with axial accelerations in cases where the magnitude of acting force exceeds its bearing capacity [4]. Dynamic bearing capacity, like the limit of vertebral strength, is determined by bone density, which correlates with the analogous parameter of the calcaneus [4]. The problem of spinal traumatism related to ejection had not been investigated in this relationship.

Our objective here was to examine the correlation between occurrence of vertebral fracture during ejection from an aircraft and density of the heel bone.

Methods

This study was conducted on the basis of data obtained from examination of flight personnel which had ejected from an aircraft by a medical commission for determination of flight fitness. The examination included the following: roentgenological examination of the cervicothoracic and lumbar spine (two projections); measurement of density of the calcaneus according to volumetric mineral content (mineralization) by the method of direct photon absorptiometry using the Studsvik (Sweden) Bone Scanner. In addition, we gathered a history, including a description of circumstances of abandoning the aircraft.

Results and Discussion

In all, we examined 27 pilots, 17 of whom constituted the control group. None had a history of fractures of the spine or other bones. The main parameters of pilots who had ejected from aircraft are listed in the Table. In all 10 cases of emergency abandonment of aircraft, the ejection seats were of the same generation with the same pyrocartridge.

Main data on pilots who ejected from aircraft

Pilot	Age, years	Height, cm	Weight, kg	Ejection position assumed	Localization of spinal fracture	Mineralization of calcaneus, g/cm^3
			With spinal fractures			
N-v	23	177	73	+	T_6	0,115
G-n	22	171	64	+	T_7	0,118
S-v	25	167	64	+	$T_{11}-T_{12}-L_1$	0,122
B-v	47	165	75	—	L_1	0,125
M-v	30	166	67	—	T_7	0,136
			Without spinal fractures			
A-v	20	175	82	+	—	0,139
Shch-v	28	173	73	—	—	0,149
Sh-n	20	176	70	+	—	0,150
A-s	30	178	82	+	—	0,163
P-v	31	176	73	—	—	0,166

The group of pilots with spinal fractures resulting from the effects of impact accelerations during ejection consisted of five cases. Typical symptoms were observed in three crew members immediately after sustaining trauma: pain with axial load and upon palpation, localized at the fracture site, difficulty in breathing, cold sweat and pallor. There were no clinical manifestations of trauma in the other two cases. The roentgenological findings were typical of a compression mechanism--fracture of the vertebral body (one or several vertebrae) with wedge-shaped deformity of the anterior part.

The role of the preparatory position was not obvious in occurrence of spinal fractures in the above cases, since they were found in three pilots who did assume the ejection position and not in two pilots who did not do so.

The age and physical development, with regard to height and weight (height/mass ratio) also failed to determine resistance to ejection accelerations.

The differences between mean weight of pilots in the groups with and without spinal fractures were unreliable ($P>0.05$) and constituted 7.4, which did not exceed 3.5% of the total mass of the seat--pilot system (~220 kg).

In the control group, mineralization of the calcaneus was in the range of 0.139± 0.163 g/cm^3 (mean 0.150±0.002 g/cm^3), i.e., it conformed with the range of variability of this parameter in pilots who ejected without spinal trauma (see Table). Mineralization of the calcaneus was reliably lower in the fracture cases.

Fractures occurred, in spite of assuming the proper position prior to ejection, in cases where mineralization was lowest (0.115-0.122 g/cm^3).

On the basis of the results in [4] and measurements of mineralization of the calcaneus in this study, it can be maintained that spinal fractures in the above-mentioned cases were attributable to strength characteristics of the spine, and assuming the proper ejection position with low mineralization of the heel bone did not preclude spinal fracture. At the same time, failure to assume the position for ejection was not associated with development of a fracture when mineralization was high enough.

Thus, low dynamic strength of the spine, as determined by mineralization of the calcaneus, could be the responsible element in the set of factors causing spinal fractures under the influence of the impact accelerations of ejection.

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UDC: 616.282-008.1-092

SIGNIFICANCE OF VESTIBULAR ASYMMETRY TO GENESIS OF VESTIBULAR DYSFUNCTION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 21 May 81) pp 64-67

[Article by V. A. Kislyakov and Yu. K. Stolbkov]

[English abstract from source] In the intact pigeons and pigeons with bilaterally cut saccular nerves, stimulation of the otolith organs did not produce asymmetric reactions from the semicircular canals, whereas in pigeons with unilaterally cut saccular nerves it resulted in the asymmetry of reactions from the semicircular canals. This asymmetry was enhanced by a combined stimulation of semicircular canals and otolith organs.

[Text] Information has been obtained from experiments with animals, as well as during manned flights, concerning change in reactivity of the vestibular system [1, 2]. The results of space flights indicate that disorders may develop in weightlessness that resemble the course of motion sickness [3, 4]. Apparently, no one questions the fact that the vestibular system is involved in the genesis of motion sickness [3-6]; however, we still observe discrepancies between the results of expert endurance test and actual flights: some individuals known to have a high level of vestibular resistance develop the space form of motion sickness in weightlessness [3, 7, 8].

Analysis of our own data [9, 10] and information in the literature [8, 11] led us to assume that vestibular dysfunction and the related space form of motion sickness may be attributable, in some cases, to latent functional asymmetry of the otolith system. A similar hypothesis had been expounded previously [12, 13]. To check this assumption, it was necessary to determine whether experimentally induced asymmetry of the otolith system leads to appearance of motor reactions similar to those noted in flight during the period of adaptation to weightlessness and in the postflight period of adaptation to earth's gravity. This article disccusses this question.

Methods

Pigeons (Columba livia) immobilized in a special stand were rotated in the horizontal plane on a stand with programmed control [14]. The lateral semicircular canals were in the plane of rotation. They were rotated in the dark on a trapezoid program: positive angular acceleration of $20°/s^2$, rotation at constant angular speed of 166°/s for 2 min (plateau) and negative angular acceleration of $20°/s^2$.

The axis of rotation passed between the labyrinths. In this case, we recorded nystagumus due to stimulation of mainly the receptors of the semicircular canals. Otolith organs were stimulated by means of shifting the otolith membranes under the influence of centrifugal force (rotation with eccentric position of the stand with the pigeon--eccentric rotation: centrifugal acceleration on the plateau constituted 0.5 G), as well as by changing the position of the pigeon's head in space (the stand with the pigeon was tilted forward, backward and to the side; the angle of inclination constituted 60°) [10]. During eccentric rotation at times of gaining and reducing speed, the receptors of the semicircular canals and otolith organs were stimulated simultaneously.

Cervical nystagmus was recorded on an N-117 loop oscillograph (10 mm/s paper feed) by deriving bioelectric potentials from the left and right rectus capitis posticus major muscles. Bioelectric potentials were recorded using silver needle electrodes (0.3 mm diameter) and amplified with a Disa 13-A-69 electromyograph.

We conducted 12 series of experiments on 12 pigeons. Each series consisted of three experiments: 1) recording cervical nystagmus in pigeons with intact saccular nerves (intact pigeons); 2) recording nystagmus after unilateral transection of the saccular nerve; 3) recording nystagmus after bilateral transection of saccular nerves. Each experiment was conducted on the day after performing the operations. The technique for severing saccular nerves (ramuli sacculi) has been described previously [9].

Results and Discussion

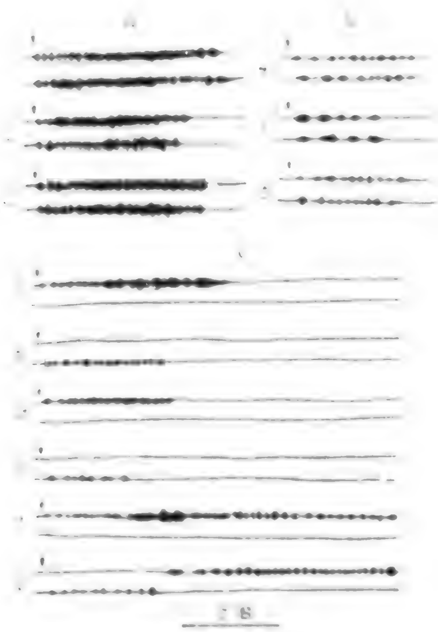
Regular muscular activity appeared in the left muscle with positive angular accelerations and clockwise rotation (to the right) and in the right muscle with negative accelerations. When the direction of rotation was changed, positive angular accelerations elicited a reaction by the right muscle and negative, by the left. The recorded activity had the appearance of bundles corresponding to the slow components of cervical nystagmus alternating with rest periods.* As can be seen in the Figure, a, electromyograms (EMG) of the right and left muscles during rotation in different directions were identical in shape and duration, and they reflected symmetry of reactions when the pigeon was rotated in both directions. After bilateral transection of saccular nerves, the reactions of the right and left muscles also remained symmetrical (see Figure, b), although they differed qualitatively and quantitatively from reactions prior to cutting the nerves [9].

To answer the question that was the purpose of this study, it is sufficient to make a quantitative analysis of the changes to which leads experimentally induced asymmetry of the otolith part of the vestibular system. Since these changes were similar in all of the pigeons, we deemed it possible to illustrate them on the EMG recorded during experiments on one of the pigeons (see Figure).

In intact pigeons, as well as those with bilateral transection of saccular nerves, rotation to both the right and left led to appearance of symmetrical reactions

*Concurrently with this activity (provided the head was firmly immobilized), one rarely records regular muscular activity (rapid component) of the contralateral muscle [14].

(see Figure, a1 and b4). With concurrent stimulation of semicircular canals and otolith organs (eccentric rotation) there was also no appearance of asymmetrical reactions (see Figure a2, a3 and b5, b6). In all of these situations, the direction of nystagmus was strictly related to the direction of deflection of the cupulae. In this sense, these reactions were adequate to the existing stimuli.



Reactions of cervical muscles to angular accelerations and centrifugal force (CFF). Time mark 5 s. Arrow shows start of rotation with positive acceleration

a) intact pigeon
b) pigeon with bilaterally cut saccular nerves
c) pigeon after unilateral transection of saccular nerves
1, 4, 7, 8) rotation in center
2, 5, 9, 10) eccentric rotation, head--tail CFF
3, 6, 11, 12) eccentric rotation, tail--head CFF
a, b (pairs 1-6) EMG of right muscle with rotation to left and of left muscle with rotation to right
c) EMG of right and left muscles with rotation to left (pairs 7, 9, 11) and right (pairs 8, 10, 12)

The findings were different in pigeons with asymmetrical function of otolith organs. Unilateral transection of saccular nerves already lead to asymmetry of reactions of semicircular canals in response to rotation in different directions (see Figure, c7, c8). There was individual variation of degree of asymmetry [9]. Moreover, in the case of combined stimulation of semicircular canals and otolith organs there was distortion of reactions: under such conditions, for example, rotation to the left was associated with appearance of nystagmus, which also continued during rotation on the plateau (see Figure, c11). With clockwise rotation, nystagmus of the left muscle occurred first, and it was then replaced by nystagmus of the right muscle, which persisted over the entire plateau (see Figure, c12). These are distorted reactions, and they are not adequate to the stimuli used. It should be noted that the above-described reactions did not appear in pigeons with unilaterally cut saccular nerves when the otoliths shifted in a caudal direction (see Figure, c9, c10), and only appeared when the otoliths shifted in a nasal direction.

The tests involving changes in spatial position of the pigeon's head yielded the following results: there was no nystagmus in any position in intact pigeons; after unilateral transection of saccular nerves, nystagmus (in the direction of the intact labyrinth) was observed only with a shift of otoliths in a nasal direction. No nystagmus was observed in any position following bilateral transection of saccular nerves.*

*There has been previous comprehensive discussion of the mechanism of occurrence of nystagmus under the influence of isolated stimulation of otolith organs [10].

Let us compare our experimental findings to data obtained from a study of oculomotor activity during orbital flights [11], as well as the results of studying vestibular function and spatial perception in the crews of the first and second missions aboard the Salyut-6 station [8].

In our experiments, asymmetry of otolith function caused asymmetry of reactions of semicircular canals. During space flight, asymmetry of oculomotor activity was observed under the influence of weightlessness [11]. After returning to earth, the cosmonauts presented asymmetry of the otolith reflex, threshold sensitivity of semicircular canals and accuracy of perception of spatial coordinates [8].

In our experiments with unilateral exclusion of saccular function, stimulation of otolith organs by means of shifting thereof under the influence of CFF, as well as change in spatial position of the head, led to nystagmus. Under weightless conditions during space flights, there was appearance of adaptive nystagmus [11].

In the case of experimentally produced asymmetry of otolith function, concurrent stimulation of semicircular canals and otolith organs elicited inadequate reactions. During space flights, there was appearance or intensification of vestibular discomfort when moving the head [8, 11]. It should also be mentioned that, after the flight, the cosmonauts developed asymmetry of the otolith reflex, and it is expressly at this time that they complained of statokinetic disorders. In the adaptation period, motor reactions were demonstrable along with autonomic disorders and illusions, and the latter appeared or became more intensive during the period of motor activity. Moreover, in one of the crew members of the first mission aboard Salyut-6, the period of adaptation to weightlessness was characterized by severe reactions (the reactions were less marked in the other cosmonauts) and expressly he had presented a preflight otolith reflex that exceeded the usually observed physiological levels [8].

Thus, it can be assumed that statokinetic disorders (and concomitant autonomic and sensory reactions) could be caused by asymmetric function of the otolith system and that there is some correlation between degree of otolith asymmetry and adverse reactions. Weightlessness does not lead to functional elimination of either the semicircular canals or otolith organs, since weight loss does not signify loss of mass and inertia [1, 15]. It cannot lead to asymmetry of vestibular function either. However, weightlessness can elicit temporary manifestation of a latent vestibular asymmetry. One of the distinctions of vestibular system function is the symmetry of reactions of the left and right labyrinths to stimuli in an effective direction that are of the same magnitude. Congenital or acquired asymmetry is compensated to some degree or other by the higher branches of the central nervous system. This corrective influence is based on afferentation from receptors of the vestibular system and is fixed in the course of individual development of the organism. With the transition to weightlessness, there is a change in afferentation from vestibular receptors, and for this reason, the corrective influence of the central nervous system, which was formed under earth's conditions, no longer compensates for vestibular asymmetry. Latent asymmetry may become overt. As a result, reactions arise upon stimulation of the vestibular system that are inadequate: information from the vestibular system conflicts with information from other sensory systems. As a result, there is development of disorders, the extreme form of which is the space form of seasickness.

Adaptation to weightlessness implies new compensation of assymetry, directed toward adequate expression of altered afferentation. There is individual variation of speed of adaptation [5, 7, 11], and it apparently depends on the level of development of compensatory and adaptive mechanisms [5]. The return to earth could lead to temporary manifestation of the latent form of vestibular asymmetry, since this is associated with another change in conditions under which the vestibular system functions.

Thus, the results of our studies and information in the literature warrant the assumption that statokinetic and associated autonomic disorders, which have been observed in some cosmonauts during the period of adaptation to weightlessness (as well as readaptation to earth), are caused by the latent form of vestibular asymmetry. This conclusion indicates that it is necessary, when conducting professional screening, not only to assess statokinetic stability and speed of formation of compensatory reactions, but to take into consideration the presence and determine the degree of latent vestibular asymmetry.

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OPTOKINETIC FACTORS AND DEVELOPMENT OF SEASICKNESS SYMPTOMS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 5 May 81) pp 67-70

[Article by L. N. Kornilova, V. A. Shakhiyeva and I. Ya. Yakovleva]

[English abstract from source] The paper describes the effects of optokinetic stimulation on the healthy man and discusses the development of motion sickness symptoms in response to the stimuli of different value and direction. The paper also indicates selective sensitivity of healthy people to optokinetic stimulation.

[Text] The experience of manned space flights has shown that the set of effects on afferent systems leading to discoordination of their function and development of "sensory conflict" occupies a significant place in onset of sensory and vestibulovegetative disorders in weightlessness. One of these factors is optokinetic stimulation--OKS (shifting of objects on earth and other objects in the visible background), to which an operator is exposed during space missions when performing work pertaining to visual observation.

The significance of OKS to formation of "sensory conflict" has been demonstrated in several works [1-10]. Cosmonauts have repeatedly reported that seeing "earth run" through the porthole made it difficult to make visual observations and, if it lasts for a long time, leads to development (or intensification) of motion sickness (MS) symptoms.

Our objective here consisted of the following: to determine the most effective OKS parameters for development of MS symptoms on earth; to study the characteristics of optokinetic nystagmus (OKN) with different intensities of OKS; to compare the resistance of healthy man to MS in the presence of OKS and recurrent vestibular stimuli.

Methods

We studied 42 men 25-45 years of age who were deemed to be in good health according to the results of otorhinolaryngological, ophthalmological, medical, neurological and otoneurological examination. We selected black bands on a white cylindrical screen, which moved in the field of vision of a subject seated motionlessly, as OKS. The distance between the screen and the subject was 120 cm, the black and white bands were 90 mm wide (5.3°). Stimulation covered the visual field horizontally over 160-170° and vertically over 80-90°. The angular rate of OKS

constituted 30, 60 and 90°/s. We used right and left movement of the vertical bands, up and down movement of horizontal bands and diagonal band movement. The frequency of band flashing at OKS rates of 30, 60 and 90°/s constituted 3, 6 and 10 bands/s, respectively.

Eye movement was recorded on a domestic electronystagmograph (time constant of the instrument 1-1.5 s, tape feeding rate 5-10 mm/s, resistance between electrodes and skin did not exceed $8 \cdot 10^3$ Ω).

We rated OKN according to the classification developed by Bod (Hungarian People's Republic). We evaluated the nature of OKN according to speed of slow phase (SSP), frequency (f) and amplitude (A). Special attention was given to demonstration and determination of physiological standards for reaction asymmetry. When using the ocular method of evaluating the optonystagmographic curve, we paid attention to the form of beats, direction, phases and rhythm. We analyzed 10-s intervals of optonystagmograms, making 20-30-s tracings in the 1st, 5th and 9th min of OKS.

MS symptoms were graded according to severity of autonomic reactions (AR) [11]. In addition, we recorded the pulse rate on the EKG, arterial pressure, cardio-intervalogram, accuracy of perception of spatial coordinates, time of appearance of illusory reactions with OKS and duration of postoptokinetic illusions. OKS was stopped upon appearance of grade I or I-II MS (MS-I and MS-I-II), or after continuous delivery for 10 min.

We started with movement of vertical bands in the frontal plane at the rate of 30°/s. In the absence of MS symptoms, the test was repeated after 20 min, but with diagonal movement of bands. If no MS symptoms appeared, the test was repeated, but with movement of horizontal bands.

There were 1-2-day intervals between testing at OKS rates of 30, 60 and 90°/s. When MS symptoms developed, the intervals between tests were 5-7 days. The level of vestibulovegetative stability was determined by the method of I. I. Bryanov [12] 7-14 days prior to [illegible] in all subjects.

We determined on 26 subjects most effective OKS parameters for development of MS symptoms. We compared individual sensitivity to vestibular and optokinetic stimuli on the basis of testing 42 subjects.

The subjects submitted to vestibular or optokinetic stimuli for 10 min with MS-0 and relative stability of tested clinicophysiological parameters were put in the stable group, and those with MS-I or MS-I-II and marked fluctuation of recorded parameters in the unstable group.

The obtained data were submitted to statistical processing with the use of Student's criterion and determination of correlations.

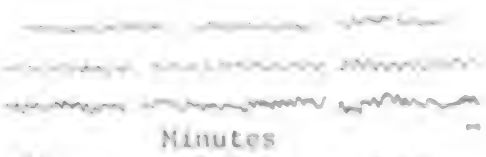
Results and Discussion

Testing endurance of optokinetic factors (26 people) revealed (see Table) that stimuli of 30, 60 and 90°/s elicited distinct motion sickness symptoms in many subjects when used for a long time (6-10 min): MS-I or MS-I-II, change in pulse, arterial pressure, cardiointervalograms, accuracy of perception of spatial coordinates.

Endurance of OKS

Rate of OKS, degrees/s	Position of bands	Stable group	Unstable group	
			MS-I	MS-I-II
30	Vertical	20	6	0
	Horizontal	21	5	0
	Diagonal	17	8	1
60	Vertical	16	7	3
	Horizontal	15	8	3
	Diagonal	10	10	6
90	Vertical	10	10	6
	Horizontal	10	10	6
	Diagonal	8	12	6

According to both autonomic and sensory reactions, the most marked symptoms of seasickness were observed with diagonal OKS at rates of 60 and 90°/s. Thus, there were distinct MS symptoms in 16 subjects at a rate of 60°/s and 18 at a rate of 90°/s. In subjects sensitive to OKS, MS was characterized by change in color of the skin, perspiration, 15-25/min increase in pulse rate and considerable elevation of tension index according to cardiointervalographic data (from 90-120 to 350-410). The sensory reactions were characterized by an increase in errors of perception of the haptic (from 1° in the background period to 5-6° with OKS) and subjective visual (from 0.5 to 3-4°) vertical. The duration of postoptokinetic illusions increased with increase in magnitude of OKS (18 s with OKS ag 30°/s, 32 s at 60 and 90°/s). The recorded clinical and physiological parameters returned to background levels 5-10 min after the 30°/s stimulus and 10-15 min after 60 and 90°/s stimulation.



Nystagmograms with different OKS rates. Top to bottom: OKS at 30, 60 and 90°/s. Time mark 1 s

Comparative analysis of optonystagmograms revealed (see Figure) that stable (in both frequency and amplitude) and well-marked OKN was observed with OKS at rates of 30 and 60°/s.

At a rate of OKS of 90°/s, there was impairment of OKN stability, manifested by interruption of nystagmus, unstable frequency and amplitude.

In subsequent studies of types and characteristics of OKN, asymmetry of reactions, physiological range thereof, as well as correlation between nature of OKN and severity of vestibulovegetative reactions with MS, we used diagonal OKS at 60°/s.

Statistical analysis of the results of these tests failed to demonstrate a correlation between nature of OKN and sensitivity to vestibular and optokinetic stimuli ($r = 0.03-0.1$ with $P<0.6$). Optomotor reactions of healthy individuals are rather stable, and they are virtually the same in stable and unstable subjects. The optonystagmograms were in the normal range according to Bodo's classification: $f = 2.49 \pm 0.5$ Hz, $A = 4.12 \pm 1.8°$, $SSP = 15.71 \pm 3.29°/s$.

Comparative analysis of optonystagmograms of several subjects revealed reliable asymmetry of parameters f ($P = 0.1$), A ($P = 0.05$) and SSP ($P = 0.01$). There was prevalence (assymetry) of reaction to the right according to SSP (average of up to

5°/s) in 21% of the subjects and to the left (to 4.1°/s) in 27%. For parameter f, we demonstrated prevalence to the right (to 1.5 Hz) in 14% and to the left in 20% (to 1.4 Hz). For parameter A, there was prevalence of reactions to the right in 1[illegible] and to the left (2.9°) in 19%.

We consider the demonstrated asymmetry to be physiological, since it is observed in healthy individuals, and the difference between all tested parameters did not exceed 10-15%. There was more frequent prevalence of a reaction with the use of OKS from left to right.

Frequency-amplitude characteristics and forms of the nystagmus curve were altered in 9 out of 42 subjects. There was a hyporeflex reaction in six of these cases and dysrhythmia in three.

The subjects were distributed as follows according to tolerance of vestibular stimuli (42 subjects): 11 were stable and 31 unstable. The distribution was different with regard to tolerance of OKS: 23 stable and 19 unstable. These data indicate that individuals with vestibular stability may be unstable to OKS and, conversely, those resistant to OKS may be sensitive to vestibular stimuli. Thus, of the 11 subjects with vestibular instablity only 7 were resistant to OKS; of the 23 resistant to OKS 16 were sensitive to vestibular stimuli.

These data enable us to recommend, for expert medical certification of flight personnel, testing of optokinetic stability (10-min diagonal OKS at the rate of 60°/s) along with determination of vestibulovegetative stability.

Apparently, it is expedient not only to determine individual sensitivity to OKS, but to take into consideration the nature of OKN. For individuals in flying professions, whose work involves accurate tracking, the hyporeflex type of OKN would be undesirable, since it is indicative of impaired perception of objects that move at high speed. The results of studies of OKN asymmetry may also be of interest to expert medical certification of flight personnel. Marked asymmetry of OKN (over 15-20%) can probably affect the precision of operator work.

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HUMAN TOLERANCE OF ROTATION AT DIFFERENT LEVELS OF HYPERGRAVITY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 3 Apr 81) pp 70-74

[Article by A. M. Genin, A. R. Kotovskaya, R. R. Galle, L. N. Gavrilova and I. Yu. Sarkisov]

[English abstract from source] The effects of acceleration of different value (up to 2 g) on the level of motion sickness, vestibular and postural reactions to rotation were studied. The experiments were carried out in a centrifuge equipped with a cabin that could be mounted at a different distance from the axis of rotation. Three experimental runs were conducted with a rate of rotation of 15.3 and acceleration values of 1.09, 1.6 and 2.0 g. Vestibular stimulation was produced by head movements of a predetermined number. It was found that with increase in the acceleration value the level of motion sickness decreased and the nystagmic reaction and balance dysfunction enhanced.

[Text] Investigation of human vital functions in rotating systems is one of the aspects of the problem of creating artificial gravity (AG) aboard space vehicles [1-3]. The results of ground-based studies can be extrapolated with adequate justification to space flight conditions if AG equals 1.0 G ["units"]. There could be a change in endurance of active presence in revolving systems in the case of hypogravity [4].

It is virtually impossible to create hypogravity conditions on earth for any length of time. For this reason, the question of nature of man's reactions while being rotated under partial gravity conditions can be answered only by conducting studies on space vehicles with AG. Indirect data concerning the direction of changes in tolerance could be obtained from ground-based studies. There is no information on this score in the literature.

Our objective was to investigate human endurance of active presence in a rotating system at different levels of hypergravity.

Methods

The studies were pursued using a centrifuge with variable arm in a special cabin 1.2×1.8×2.0 m in size (Figure 1). The distinction of this equipment is that it was possible to alter the position of the cabin in relation to the axis of rotation

and in relation to the horizontal plane. Thus, a change in gravity was produced by altering the radius of rotation rather than angular velocity. In all cases, the resultant [equally effective] vector was perpendicular to the plane of the cabin floor. Since the same angular velocity was used, the levels of precession and Coriolis accelerations depended only on the movements made by subjects during rotation. Adherence to a standard regimen of motor activity provided relative constancy of vestibular stimuli in the presence of different gravity levels. Thus, conditions were provided for special evaluation of the effect of gravity level on tolerance of rotation.

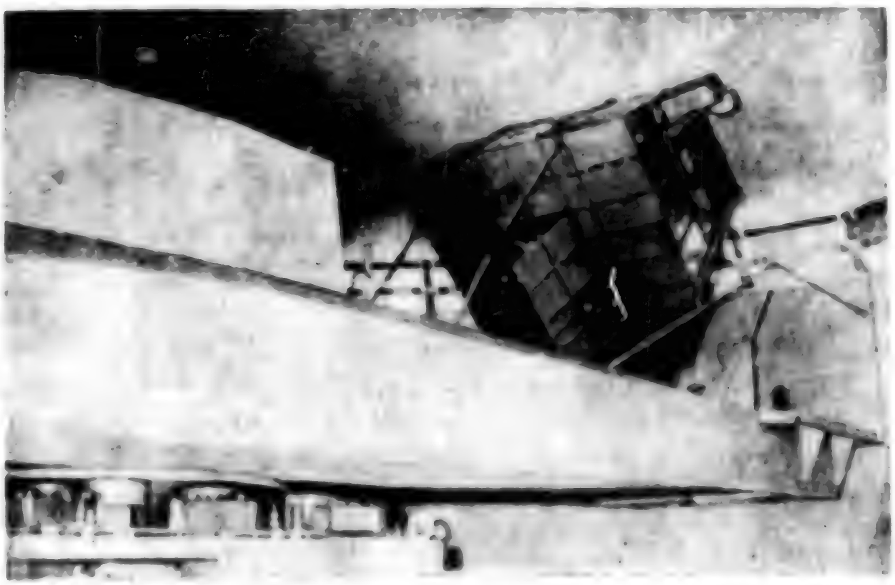

Figure 1. View of centrifuge with cabin

1) centrifuge arm*
2) cabin
3) cabin door
4) television camera
5) current pick-up device

The cabin is equipped with illumination, ventilation, communication and television systems to monitor the subject's condition, as well as a system for collecting and transmitting physiological information on recording equipment. The subject was seated in a chair facing the rotation axis.

Three series of tests were conducted at a speed of 15.3 r/min with the cabin mounted at different distances from the rotation axis. One rotation lasted 60 min. In the first series, the equally effective [resultant?] component

*Translator's note: None of the keyed numbers is visible on the photograph.

constituted 1.09 G, and in the second and third hypergravity constituted 1.6 and 2.0 G, respectively. During rotation, the subjects performed graded nodding motions with the head in a radial direction at the rate of 1 movement per 3 s (12 slow nods) and at the rate of 1/1 s (up to 100 rapid nods). The precession accelerations that this was associated with constituted a mean of 0.42 and 1.26 rad/s^2. Endurance of 60-min rotation was assessed chiefly on the basis of presence and severity of signs of motion sickness. For this purpose, we used the subjects' reports about their well-being, results of monitoring their behavior and performance of vestibular loading test, as well as number of bouts of vomiting. Clinical symptoms of motion sickness were evaluated by the system proposed by one of the present authors [5]. A grade was given 7 times during the 60 min of rotation. The totaled grades were used as the quantitative indicator of tolerance of rotation as a whole.

In addition, we recorded heart rate, arterial pressure and respiration rate during rotation. We assessed vestibular function according to nystagmus, which was recorded electrographically while the subjects performed graded slow head movements. To assess equilibrium in vertical position we used stabilography.

A total of 22 essentially healthy men, 23-40 years of age, were involved in the tests, and each of them participated in rotation at different gravity levels three times at intervals of at least 1 week.

The obtained data were submitted to statistical processing by the Student method.

Results and Discussion

In the presence of 1.09 G hypergravity (series I), during rotation the subjects developed symptoms of motion sickness, the severity of which varied individually. Sensory reactions appeared from the first minutes of rotation. During voluntary movements they were most often in the form of vague dizziness and with graded head movements, in the form of rotation illusions. In some cases, the sensory reactions were so severe that they were associated with brief loss of spatial orientation.

So-called vestibulovegetative symptoms appeared 10-15 min after the start of rotation: increased salivation, perspiration, sensation of fever or chills, nausea to the point of vomiting bouts. During the second half of the rotation period, the subjects became drowsy, sluggish, presenting headache and other "central" symptoms of motion sickness.

Analysis of the severity of motion sickness according to one of the chief symptoms (nausea) revealed that it was present in 15 subjects, in 7 of whom it led to vomiting. Eight subjects were unable to perform the entire scheduled graded vestibular exercise, which included up to 100 rapid nods of the head, because of distinct worsening of their condition (intensification of motion sickness symptoms).

Motion sickness symptoms regressed with increase in gravity to 1.6 and 2.0 G (series II and III): the number of subjects complaining of nausea diminished to 13, while only 2 in each series had vomiting bouts. The number of instances of failure to perform the vestibular loading test with nodding decreased by one-half.

Figure 2 illustrates graphically the quantitative index of tolerance of 60-min rotation as a function of gravity level. According to the mean data, this index, which is based on the grade given to severity of motion sickness, had a tendency to decline

[illegible] gravity increased in all groups (curve 1). Since there was individual variation of severity of motion sickness over a significant range, we selected two groups of six men from the total number of subjects. The first group consisted of subjects with susceptibility to motion sickness. They developed moderate or severe manifestations of motion sickness when performing graded vestibular exercise during rotation at minimal gravity (1.09 G). The second group consisted of subjects in whom the vestibular load under the same conditions led to insignificant manifestations of motion sickness.

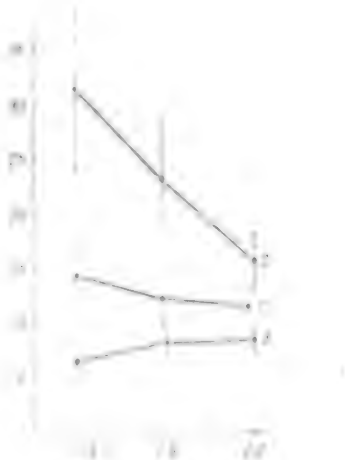

Figure 2.
Severity of motion sickness as a function of level of hypergravity. X-axis, hypergravity level (units); y-axis, severity of motion sickness (grade; M±m)

1) mean rating (grade) for all subjects
2, 3) the same for the group of subjects susceptible to motion sickness and resistant to vestibular stimuli, respectively

With increase in gravity, the subjects sensitive to motion sickness presented distinct worsening of endurance of rotation: the overall grade dropped reliably (curve 2). In subjects resistant to vestibular stimuli, the same parameter showed virtually no change with increase in gravity (curve 3).

To sum up analysis of clinical manifestations of motion sickness, it can be noted that good endurance of rotation persisted at all gravity levels up to 2.0 G in subjects resistant to vestibular loads, whereas in those susceptible to motion sickness hypergravity led to a substantial decrease in severity of motion sickness and, consequently, better tolerance of rotation.

The heart rate, arterial pressure and respiratory rate changed insignificantly during rotation. We can merely mention some increase in heart rate at hypergravity (2.0 G). While this parameter was in the range of 72-80/min in the first series, the mean heart rate constituted 70-90/min in the third. Similar insignificant changes in the cardiovascular system were observed with exposure of man to low level accelerations [6].

Analysis of nystagmograms revealed that the horizontal component of nystagmus at the final phase of slow nods (when straightening up) was more distinct in all of the test series. With increase in gravity, the nystagmic reaction was appreciably stronger, particularly with respect to number and amplitude of nystagmic waves. A highly reliable increase in this parameter was observed, as compared to the reaction at 1.09 G gravity (Figure 3). The typical nystagmograms of one of the subjects, which were obtained in the three series of tests can serve as an illustration of these nystagmic distinctions (Figure 4).

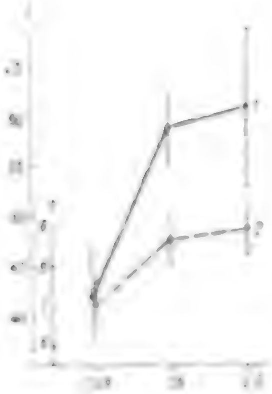

Figure 3.
Number of nystagmus beats and amplitude as a function of level of hypergravity. X-axis, level of hypergravity (units); y-axis:

1) number of beats (M±m; curve 1)
2) amplitude of nystagmus, degrees (M±m; curve 2)

Equilibrium, which was assessed according to stabilographic parameters of stability in vertical position, was impaired during rotation, and this impairment became more marked with increase in gravity. The causes of worsening of equilibrium during rotation under hypergravity conditions require further investigation. Perhaps, the direct effect of increased body weight on man's postural reactions played some part in these changes.

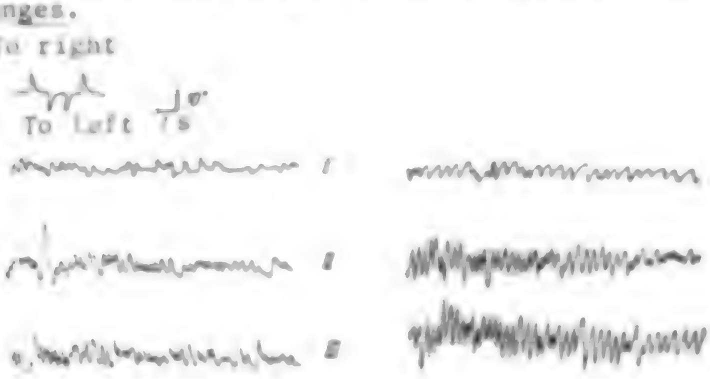

Figure 4. Electronystagmograms (horizontal component) recorded during slow nods against the background of rotation at different levels of hypergravity. The Roman numerals refer to test series.

a) nodding b) straightening up

Thus, our results warrant the conclusion that with increase in gravity to 2.0 G, provided its vector is parallel to the longitudinal axis of the human body, there is improvement of endurance of rotation, evaluated chiefly by the severity of motion sickness. This was manifested in particular in subjects susceptible to motion sickness. At the same time, we demonstrated intensification of the nystagmic reaction under the influence of adequate stimulation of receptors of semicircular canals under hypergravity conditions, as well as worsening of equilibrium.

The difference in direction of changes is indicative of different mechanisms of effects of the gravity environment on the syndrome of motion sickness, vestibulo-oculomotor and postural reactions. As we know, repeated stimulation of labyrinthine receptors is the triggering mechanism of motion sickness. However, the most diverse functional systems are involved in the mechanisms of its development [7].

For this reason, hypergravity affects severity of motion sickness probably via systems other than the vestibular (in such a case, the demonstrated changes would be in the same direction). In particular, there are data indicative of the inhibitory effect of the system of the motor analyzer on manifestations of motion sickness [8], and the functional state of this analyzer does not necessarily change with increase in gravity.

The changes in nystagmus at different levels of gravity are based on vestibular mechanisms, namely, intraanalyzer correlations between the cupular and otolith parts of the vestibular analyzer. Questions of interaction between cupular and otolith systems, in particular, the effect of otolith stimulation on nystagmus, have been studied for many years. However, there are contradictory opinions on this score in the literature [9-11], chiefly due to the use of different methodological approaches to this problem. The methodological approach used here (change in gravity without change in magnitude of vestibular stimulation) enabled us to answer this question unequivocally. Stimulation of otolith receptors due to increased gravity has an activating effect on nystagmus induced by adequate stimulation of receptors of semicircular canals. In other words, nystagmus is enhanced if exposure to angular accelerations occurs against a hypergravity background.

The data obtained from this study may be of practical value to medical support of many future space flights with AG. There is no reason to expect poorer endurance of rotation under hypogravity conditions by individuals who tolerate well a long stay in rotating systems in earth's gravity. At the same time, on the basis of the hypothesis of qualitative similarity of reactions to changes in gravity in different directions [12], it may be assumed that individuals who are susceptible to motion sickness during rotation under earth's conditions will tolerate it all the more, the lower the level of AG. This means that under hypogravity conditions there will be greater demands made of spacecraft crews with respect to their resistance to vestibular factors.

On the whole, one should strive to have AG of 1.0 G when using rotation with angular accelerations that do not elicit vestibular disorders of the motion sickness type [4, 5].

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COMPARATIVE EVALUATION OF PRESSURE CHAMBER CONDITIONING AND MAN'S ADAPTATION TO HYPOXIA AT HIGH ALTITUDE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 5 May 81) pp 74-77

[Article by A. Yu. Katkov, R. N. Chabdarova, N. V. Pravetskiy, S. A. Vtoryy, V. V. Lenskiy and A. A. Titov]

[English abstract from source] It was demonstrated that a 3-day pressure chamber training may increase the maximum tolerable "altitude" at rest from 8,600-8,900 m (depending on the onset rate of hypoxia) to 9,600 m. After pressure chamber training the maximum tolerable "altitude" increased from 8,200 m to 9,200 m, when exercising in a bicycle ergometer at 200 kgm/min and continuously ascending at a rate of 20 m/sec. A similar antihypoxic effect was also provided by a 7-day high altitude adaptation. Using polarographic measurements of oxygen tension in the skin, it was found that adaptation to hypoxia induced a more pronounced oxygen decrease at high altitudes. This can be attributed to a more distinct blood redistribution, i.e., a better blood supply to the vital organs at the expense of peripheral tissues.

[Text] Of the methods described in the literature for accelerated conditioning of animals to hypoxia, the most effective is a 3-day stay in a pressure chamber [1]. We submit here the results of testing the antihypoxic efficacy of an analogous method of conditioning man and the results of comparing it to parameters of antihypoxic resistance under the influence of high-altitude adaptation.

Methods

There were 14 subjects involved in this study, 7 of whom underwent 3-day conditioning in a pressure chamber with 15-fold daily change in "altitude" on the following schedule: "ascent" at the rate of 20 m/s without additional supply of oxygen to an "altitude" of 5000 m, staying for 2 min 10 s first at this "altitude," then at "altitudes" of 6000, 7000, 8000 and 9000 m, depending on how the subjects felt. The "climb" from one "plateau" to another was effected at the same rate, i.e., within 50 s. At the maximum "altitude" of conditioning "ascent," when so instructed the subject put on an oxygen mask and breathed oxygen during the "descent" (at the rate of 20 m/s) to 5000 m. This was followed by an analogous change in "altitudes." High-altitude adaptation of the other group of subjects (7 people) occurred in the

Table 1. Changes in man's endurance of acute hypoxia under the influence of pressure chamber conditioning and adaptation in the mountains

Time of examination	Subject	Gradually increasing hypoxia			"Ceiling" with rapidly increasing hypoxia, m	
		"ceiling" m	"reserve of time" at maximum "altitude"	total time of exposure to hypoxia, min	at rest	exercise
Before pressure chamber conditioning	S.	8 000	8 min 40 s	43	8 700	7700
	G.	9 000	2 " 48 "	47	9 100	8500
	D.	8 000	5 " 28 "	39	9 200	8300
	A.	8 000	3 " 7 "	37	9 000	8500
	B.	9 000	2 " 37 "	47	9 100	8500
	R.	9 000	4 " 47 "	49	8 600	8200
	B-iy	9 000	3 " 48 "	48	8 900	7700
$M \pm m$		8 600±200		44±1.8	8 900±90	8200±140
After pressure chamber conditioning	S.	9 000	6 " 22 "	50	9 600	9300
	G.	9 000	7 " 22 "	51	9 500	8900
	D.	10 000	1 " 7 "	55	9 700	9100
	A.	9 000	5 " 18 "	49	10 000	9300
	B.	10 000	3 " 5 "	57	9 500	9500
	R.	10 000	3 " 9 "	57	9 500	[illegible]
	B-iy	10 000	1 " 8 "	55	9 600	9500
$M \pm m$		9 600±210;		54±1.3.	9 600±70;	9200±100;
P		<0.002		<0.001	<0.001	<0 001
Before mountain adaptation	K.	8 000	38	35	9 300	8000
	Zh.	7 000	40	25	9 100	7600
	S..	9 000	2 " 21 "	47	8 800	7800
	T.	8 000	5 " 22 "	40	9 200	8300
	B.	9 000	46 "	45	9 900	8600
	S-yn	9 000	9 " 10 "	53	9 600	8300
	M.	9 000	48 "	45	8 800	7600
$M \pm m$		8 400±300		41±3.4	9 200±150	8000±150
After mountain adaptation	K.	9 000	5 " 20 "	50	10 600	[illegible]
	Zh.	9 000	5 " 36 "	50	9 100	8100
	S.	9 000	4 " 24 "	49	9 200	8500
	T.	9 000	3 " 10 "	47	9 700	9200
	B.	10 000	Over 10 min	64	10 200	9300
	S-yn	10 000	1 min 39 s	56	10 500	8900
	M.	10 000	8 " 25 "	63	10 500	8600
$M \pm m$		9 400±200		54±2.6	10 000±240	8900±190
P		<0.02		<0.02	<0.02	<0.01

mountains of the Caucasus on the following program: 1st day--stay at altitude of 3500 m; next 6 days--4200 m, i.e., total stay in the mountains constituted 7 days. Just prior to and after pressure chamber conditioning, as well as before and on the 7th-10th day after mountain adaptation, we determined endurance of gradually increasing hypoxia by subjects in the pressure chamber during successive 10-min stays at "altitudes" of 5000, 6000, 7000, 8000, 9000 and 10,000 m [2]. We also tested tolerance of rapidly increasing hypoxia in the chamber. The subject was "raised" continuously (at the rate of 20 m/s) without additional oxygen suply, first at rest and then (30 min after "descent") with continuous exercise on a bicycle ergometer (200 kg-m/min). In both cases, starting at an "altitude" of 7100 m, the subject had to give signals with the fingers of his right hand to indicate every 100 m of his "climb." Determination was made of the maximum "altitude," at which he lost the ability to perform this task. During the tests, we recorded the heart

Table 2. Effect of pressure chamber conditioning and mountain adaptation on dynamics of O_2 tension in alveolar air and skin during gradually increasing hypoxia

Time of study	Parameter	Before "ascent" in pressure chamber	At pressure chamber "altitude" of (m): 5000	6000	7000	8000	9000	10 000	At moment of stopping test in the chamber
Before	O_2 tension in alveolar air	102 ± 2.1	45 ± 1.4	40 ± 2.0	35 ± 1.9	29 ± 2.0	—	—	—
	Same in skin	33 ± 2.2	20 ± 2.1	17 ± 2.3	15 ± 1.6	11 ± 1.5	—	—	9 ± 1.9
After condition. in chamber	Same in alveolar air	107 ± 1.6	49 ± 1.2	42 ± 1.4	36 ± 1.1	22 ± 1.7	27 ± 0.9	—	—
	Same in skin	39 ± 1.8	22 ± 2.0	15 ± 2.1	11 ± 1.5	6 ± 1.1	3 ± 1.2	—	3 ± 0.8
	P_1	>0.05	<0.05	>0.25	>0.5	>0.25	—	—	—
	P_2	>0.05	>0.5	>0.5	<0.05	<0.05	—	—	<0.02
Before	O_2 in alveolar air	105 ± 0.7	47 ± 1.3	42 ± 1.1	35 ± 1.7	31 ± 2.4	—	—	—
	Same in skin	36 ± 4.5	14 ± 2.9	11 ± 1.9	10 ± 2.1	10 ± 0.7	—	—	7 ± 1.1
After mountain adaptation	Same in alveolar air	106 ± 1.2	53 ± 1.3	44 ± 1.3	39 ± 1.4	33 ± 1.3	29 ± 0.6	25	—
	Same in skin	36 ± 2.9	16 ± 2.5	14 ± 2.3	12 ± 1.5	6 ± 2.6	4 ± 3.0	0	5 ± 1.9
	P_1	>0.25	<0.01	>0.25	>0.05	>0.25	—	—	—
	P_2	—	>0.5	>0.5	>0.5	>0.1			>0.05

Note: P—reliability of changes as compared to values before adaptation to hypoxia (P_1—for O_2 tension in alveolar air and P_2 for O_2 tension in the skin).

rate (HR), respiration rate (RR), arterial pressure (AP) and O_2 tension in the skin of the left forearm (polarographic method). A discrete method was used to take samples of alveolar air on the ground and at the end of the 10-min "plateaus" in the chamber. We analyzed morphological composition of peripheral blood under normal barometric pressure.

Results and Discussion

On the 1st day of pressure chamber conditioning, the maximum "altitude" at which the subjects were able to put on the oxygen mask ranged from 8000 to 9000 m, but already on the 2d day of conditioning it was 9000 m for all subjects. Both pressure chamber conditioning and adaptation in the mountains were not associated with any appreciable changes in quantity of erythrocytes, hemoglobin, leukocytes and leukocyte formula, which is probably attributable to the short duration of these procedures.

Table 1 lists the results of testing the effect of conditioning in the pressure chamber and adaptation in the mountains on human endurance of acute hypoxia. Table 1 shows that there was virtually the same increase in resistance to hypoxia under the influence of pressure chamber conditioning as under the influence of mountain adaptation. An analogous enhancement of man's tolerance of gradually increasing hypoxia in a pressure chamber was observed in the case of 10-day conditioning in the chamber by the method of Ye. A. Kovalenko [3]. Approximately the same increase in resistance to high altitude was observed in mountain climbers following a 1.5-month stay at high altitudes climbing to peaks of 7000-8000 m [4, 5]. All this indicates that the antihypoxic efficacy of brief "pulsed" modes of pressure chamber conditioning may be as good as longer adaptation in the mountains, but the greater resistance to hypoxia lasts longer after adaptation to mountains [6].

There were no appreciable changes in HR, RR or AP reactions to acute hypoxia after pressure chamber conditioning, whereas after mountain adaptation there was less marked tachycardia and change in AP with

gradual buildup of hypoxia. Thus, while HR rose from 65±3.5 to 96±5.8/min and AP changed from 120±2.4/80±3.9 to 140±5.0/75±2.5 mm Hg prior to adaptation to high altitude during "climb" in pressure chamber to an "altitude" of 8000 m, after mountain adaptation the figures were 62±1.7 to 85±4.1/min and 115±3.3/70±5.2 to 115±3.2/65±10.0 mm Hg, respectively. There was a tendency toward elevation of O_2 tension and decline of CO_2 tension in alveolar air under hypoxic conditions after both pressure chamber conditioning and mountain adaptation, as compared to the levels demonstrated before the start of adaptation. With reference to skin O_2 tension, the opposite pattern was demonstrated. As can be seen in Table 2, O_2 tension of the skin at "altitudes" of 7000 and 8000 m was lower with statistical reliability after chamber conditioning than before the start thereof. There was a more marked difference between O_2 tension in the skin before and after pressure chamber conditioning at the moment the test was stopped in the case of gradually increasing hypoxia. The same tendency toward more marked decline of skin O_2 tension in the presence of extreme degrees of acute hypoxia was observed, though less distinctly, after mountain adaptation. In all likelihood, the demonstrated reaction of skin O_2 tension to hypoxia is attributable to the more marked spasm of peripheral microvessels under the influence of conditioning to hypoxia. If we consider the fact that such a spasm under hypoxic conditions makes it possible to improve blood supply to the brain and heart, the desirability thereof becomes obvious.

In our opinion, the antihypoxic effect of both pressure chamber conditioning and mountain adaptation is attributable, on the one hand, to improved delivery of oxygen to tissues and, on the other hand, redistribution of blood intended to improve supply of blood to vital organs at the expense of peripheral tissues.

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ACTIVITY OF SOME RAT LIVER ENZYMES FOLLOWING FLIGHT ABOARD COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 18 Dec 79) pp 77-80

[Article by Š. Németh and R. A. Tigranyan (CSSR, USSR)]

[English abstract from source] After the 18.5-day flight onboard the biosatellite Cosmos-936, the activity of 6 glucocorticoid-activated enzymes in the rat liver was investigated. It was found that at R+0 activities of tyrosine aminotransferase and tryptophan pyrolase, as well as fructose-1,6-diphosphatase, glucose-6-phosphatase, aspartate aminotransferase and alanine aminotransferase increased. The two former enzymes react rapidly (within several hours) to an increase in the glucocorticoid level, whereas those latter react only to a continuous prolonged effect of glucocorticoids. These increases were paralleled by a growth in the glycogen concentration in the liver. The findings indicate that during the flight the rats underwent a chronic stress induced by weightlessness.

[Text] Administration of glucocorticoid hormones increases the activity of several enzymes in the rat liver. One group of enzymes, in particular, phosphoenolpyruvate carboxykinase (PEPCK, EC 4.1.1.32), tyrosine aminotransferase (TAT, EC 2.6.1.5) and tryptophan pyrrolase (TP, EC 1.13.11.11), show an increase in activity within a few hours, whereas the reactions of other enzymes, namely, fructose-1,6-diphosphatase (FDP, EC 3.1.3.11), glucose-6-phosphatase (G-6-P, EC 3.1.3.9), aspartate aminotransferase (AsAT, EC 2.6.1.1.) and alanine aminotransferase (AlAT, EC 2.6.1.2), require exposure to hormones for many days [1].

The activity of enzymes of the liver with rapid reactions also increases under stress. Thus, in the case of immobilization stress, there was an increase in activity of TAT [2], TP [3] and PEPCK [4]. It has also been demonstrated that TAT and TP activity under such stress is increased only by glucocorticoids [5]. With recurrent stress, there is an increase in activity of AsAT and AlAT, which require the prolonged influence of hormones; in adrenalectomied rats, the activity of these enzymes did not increase, and this confirms the role of glucocorticoids in this reaction [1]. The above data indicate that enzymes whose activity increases rapidly are good indicators of acute stress, whereas activation of AsAT and AlAT, which require the prolonged action of glucocorticoids, is indicative of chronic stress.

We applied these theses to an experiment aboard the biosatellite, Cosmos-936.

Methods

The tests were conducted on male Wistar-SPF (Bratislava, CSSR) rats who had flown in space aboard Cosmos-936 for 18.5 days. Tables 1 and 2 list the characteristics of the rats and their diet.

Enzyme activity was measured in a homogenate (G-6-P [7]) or supernatant after centrifuging at 15,000 G (TAT [8], TP [9], FDP [10], AsAT and AlAT [11]). In addition we determined glycogen concentration in the liver [12] and assayed protein in incubated material [13].

Table 1. Data on Cosmos-936 animals

Group and number of animals	Feed intake, g/day	Body weight, g	Liver weight, g	Protein in supernatant of 10% liver homogenate, mg·mℓ$^{-1}$
1. Flight--weightlessness (5)	54.5	304.4±19.6	13.6±0.9	10.8±0.4
2. Flight--centrifuge (4)	35.2	258.7±4.9	10.2±0.8	11.9±0.4
3. Synchronous experiment (5)	45.5	288.0±6.0	11.1±0.2	12.4±0.5
4. Synchronous experiment--centrifuge (5)	35.0	274.0±6.4	10.7±0.5	12.5±0.4
5. Vivarium control (5)	40.0	307.0±6.4	10.5±0.4	11.8±0.3
6. Flight--weightlessness (5)	51.4	331.0±7.5	9.5±0.5	14.6±0.7
7. Flight--centrifuge (5)	39.4	350 0±7.7	10.9±0.5	14.1±0.3
8. Synchronous experiment (5)	54.8	337.0±6.0	9.4±0.4	15.2±0.3
9. Vivarium control (4)	40.0	332.0±3.7	9.8±0.2	14.9±0.2

Note: The number of animals is given in parentheses. The 1st-5th groups were decapitated 6 h after landing and the 6th-9th groups 25 h after landing. The weight of the animals is shown after decapitation. The 5th and 9th groups were fed by hand and the others automatically during the flight; after landing all groups were given 40 g feed by hand.

Results and Discussion

TAT and TP activity increased immediately after the flight (Figures 1 and 2), which was indicative of acute stress, apparently related to landing of the biosatellite. There was also an increase (when enzyme activity was scaled to 1 g liver protein) in AlAT activity (see Figure 1), which could be indicative of onset of chronic stress. This is also confirmed by the increase in activity of AsAT, AlAT, FDP and G-6-P, as compared to the vivarium control (see Figure 2). True, an increase in AlAT and G-6-P activity occurred in both groups of animals in the synchronous experiment, which can most likely be attributed to the effect of stress related to manipulations with these animals.

The increase in AsAT and AlAT activity is apparently related to activation of processes of gluconeogenesis; this was indicated by the increase in FDP and G-6-P

activity (see Figure 2), and they are the key enzymes of gluconeogenesis. The rise in glycogen level in the liver of rats exposed to weightlessness (Figure 3) was also indicative of increased gluconeogenesis. In all likelihood, the high concentration of glycogen was the cause of increase in weight of the liver and decrease in protein concentration in this group of animals (see Table 1).

Table 2. Characteristics of animal diet (based on 40 g daily allowance, 60% moisture)

Nutrient	Quantity, g	Minerals	Quantity, mg	Vitamins	Quantity
Protein	3.06	Sodium	60.9	B_1	64.8 μg
Fat	1.79	Chloride	15.5	B_2	62.4 μg
Carbohydrate	9.61	Potassium	67.1	B_3	240.0 μg
		Phosphorus	86.3	B_6	50.5 μg
		Calcium	84.3	PP	493.6 μg
		Iron	3.19	E	1380.0 μg
		Zinc	0.08	A	20 IU
		Iodine	0.07	D	6 IU
		Copper	0.08	K	16.0 μg
		Cobalt	0.008	B_{12}	0.48 mg
		Fluorine	0.13	B_{15}	16.0 μg
		Aluminum	0.008	Folic acid	32.0 μg
		Magnesium	6.96	Inositol	800.0 μg
		Sulfur	11.17	p-aminobenzoic acid	800.0 μg
		Manganese	0.90	Choline	16,000.0 μg

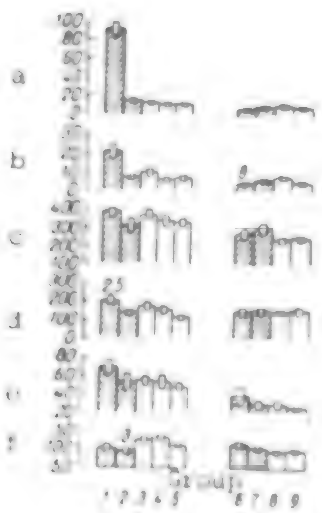

Figure 1.
Activity of liver enzymes scaled to 1 g protein
Here and in Figure 2:
a, c-f) TAT, AsAT, AlAT, FDP and G-6-P, respectively ($\mu M\ g^{-1} \cdot min^{-1}$)
b) TP ($\mu M\ g^{-1} h^{-1}$).
The features of the groups are listed in Table 1. The numbers over the columns refer to the group, as compared to which reliable data were obtained (P<0.02). TAT and TP activity was reliably increased immediately after landing (1st group), as compared to other groups.

Enzyme activity and liver glycogen concentration 25 days after the flight did not differ from these levels in the vivarium control (see Figures 1, 2 and 3), with the exception of diminished TAT activity in flight animals submitted to weightlessness (see Figure 2).

Figure 2.
Liver enzyme activity scaled to 1 g body weight

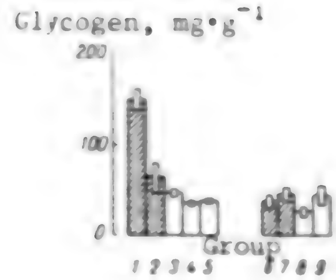

Figure 3.
Glycogen content of liver. Concentration of glycogen is reliably elevated in the first group, as compared to others

The activity of hepatic enzymes can change (aside from increased concentration of glucocorticoids in blood) as a function of quality and quantity of food intake. Starvation and excessive protein in food increase AsAT, AlAT [14] and G-6-P [15] activity in the liver. The animals in different groups did not consume the same amounts of feed. Intake was highest in the flight group of animals immediately after completion of the flight (see Table 1). The increased feed intake should have resulted in weight gain; however there was no reliable increase in average weight of the rats. This means that increased food intake could not be the cause of the demonstrated changes. For this reason, the changes demonstrated in flight animals immediately after landing can apparently be attributed only to the influence of the elevated levels of glucocorticoids secreted as a result of stress.

In our opinion, development of chronic stress was related to the effects of weightlessness, as indicated by the lack of changes in activity of tested enzymes in the liver of rats submitted to centrifugation. The obtained data are entirely consistent with the results of our assay of blood plasma corticosterone concentration.

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CATECHOLAMINE CONTENT OF RAT BLOOD AFTER FLIGHT ABOARD COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 19 May 80) pp 80-83

[Article by R. Kvetňansky and R. A. Tigranyan (CSSR, USSR)]

[English abstract from source] The content of epinephrine and norepinephrine was measured in plasma of the rats flown onboard the biosatellite Cosmos-936 in the weightless state and under artificial gravity. With respect to the norepinephrine content there was no difference between the two flight groups, while its level in the flight rats was higher than in the ground-based controls. The epinephrine content in the flight rats remained essentially unchanged. These data give evidence that a prolonged exposure to weightlessness is not a stressogenic factor as related to the sympathoadrenal system.

[Text] Heretofore, only catecholamine (CA) and enzymes of their metabolism in the adrenals [1] and hypothalamus [2] were analyzed as indicators of adrenosympathetic activity in space experiments on rats; however, the blood level of CA is the best indicator of activation of the adrenosympathetic system. Fluorometric assay of blood CA is relatively inaccurate, since the data are on the boundary of sensitivity of this method when a large amount of plasma is used. The highly sensitive radioenzymatic method of assaying CA makes it possible to determine the levels of epinephrine (E) and norepinephrine (NE) in 0.2 mℓ samples of both human and animal blood plasma, in particular, rats [3-5]. Using this method, it was demonstrated that E and NE levels in plasma rose significantly in rats submitted to both intensive [6] and mild [7] stress.

Our objective here was to assay blood plasma E and NE levels in rats after a space flight aboard Cosmos-936 biosatellite in order to assess stressogenicity of long-term weightlessness.

Methods

This study was conducted on male Wistar-SPF (Bratislava, CSSR) rats flown for 18.5 days aboard the Cosmos-936 biosatellite. The experimental conditions are described by Ye. A. Il'in et al. [8].

Immediately after decapitating the rats, we collected blood in heparinized tubes; 200 μℓ plasma was frozen after centrifuging to assay CA, and plasma was transported and stored in this state for several weeks, until it was analyzed. After defrosting, protein was removed from plasma by addition of 200 μℓ 0.6 N $HClO_4$ containing 2% EDTA and 0.2% $MgCl_2 \cdot 6H_2O$. After centrifuging (3000 G), 200 μℓ supernatant was incubated for 90 min at 37°C with 200 μℓ mixture containing 0.5 mg dithiotreytol [?], 5 μℓ 3 M $MgCl_2 \cdot 6H_2O$, 175 μℓ 2 M tris (containing 31.8 mM EDTA) pH 9.6, 5 μℓ adenosyl-L-methionine-S (methyl-^3H), 2.5 μCi (specific activity 6.9 μCi/M) and 15 μℓ partially purified catechol-O-methyltransferase.

After incubation, the reaction was stopped in an ice bath by addition of 400 μℓ solution consisting of 350 μℓ boric buffer pH 8.0 and 50 μℓ nonradioactive carrier (25 μg each of metanephrine and normetanephrine in 0.01 N HCl). After addition of 50 μℓ 1.5% tetraphenyl borate, the appearing labeled methyl catecholamines were extracted with 10 mℓ toluene and isoamyl alcohol (3:2); after freezing and separation of phases, the organic extract was reextracted in 500 μℓ 0.1 M acetic acid. The specimens were then eluated in 2 mℓ toluene and isoamyl alcohol (3:2), lyophilized overnight, the residue dissolved in 50 μℓ mixture of methanol and 0.001 N HCl (4:1), and transferred to silica gel film (Merck 60F-254). The film was developed for 2.5 h in a system containing 72 mℓ tetraamyl alcohol, 24 mℓ benzene and 36 mℓ 40% methylamine; after localization of spots in ultraviolet light, the E and NE segments were scraped off into scintillation vials, amines were eluated in 1 mℓ 0.05 N NH_4OH and acidulated by addition of 50 mℓ 4% $NaIO_4$ at room temperature. The reaction was stopped after 5 min by addition of 50 μℓ 10% glycerin; the obtained vanillin was extracted with 10 μℓ mixture of toluene and Liquifluor (1000:50) in scintillation vials after addition of 200 μℓ 1 N acetic acid, and radioactivity of samples was measured. Internal E and NE standards (0.5 ng) were added to average plasma samples and the entire analysis was performed on these samples. Blind samples consisted of 200 μℓ supernatant from an average plasma sample free of proteins and 200 μℓ mixture incubated in a separate test tube; this mixture was mixed with 200 μℓ supernatant only after completion of incubation and addition of 400 μℓ 1 M boric buffer and unlabeled carrier. The sensitivity of this method is greater than 5 pg CA in the analyzed sample. This method is our modification of several techniques for demonstrating CA in plasma [3-5].

The results we are submitting are the average data for 4-5 samples; statistical reliability was determined by the t test of Student.

Results and Discussion

Immediately after the flight, plasma NE levels rose reliably in both flight groups of rats, as compared to the vivarium control and corresponding groups in the synchronous experiment. Interestingly enough, the plasma NE level rose to the same extent in animals exposed to artificial gravity (AG) in flight as in weightless animals. No differences were noted between the parameters of different control groups (vivarium control, synchronous experiment, short-arm centrifuge). NE level in flight rats did not differ from control values 25 days after landing; however, blood plasma NE concentration was elevated in all control groups of rats (Figure 1).

Plasma E content was not increased in flight groups of rats, as compared to the vivarium control; a reliable difference was demonstrated only in flight animals exposed to weightlessness, as compared to the parameters of animals in the synchronous control. There was no significant difference between findings on the

different control groups. Plasma E level 25 days after the flight did not differ in flight rats from that of the control, but in this case plasma E concentration was elevated in all control groups (Figure 2).

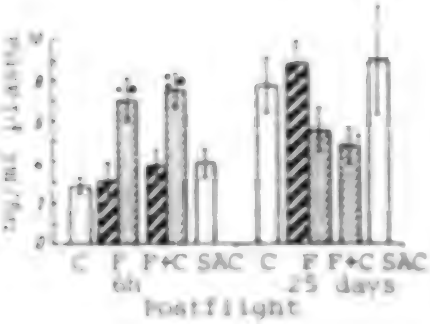

Figure 1

Plasma NE level in rats flown aboard Cosmos-936 biosatellite.

Here and in Figure 2:

C) vivarium control

F) flight

F+C) flight + centrifuge

SAC) short-arm centrifuge

There were 5 animals in each group; * refers to P<0.02 and ** to P<0.01, as compared to vivarium control; dots refer to P<0.05, as compared to synchronous control. Thin-line hatching indicates flight and bold-face hatching indicates the synchronous experiment.

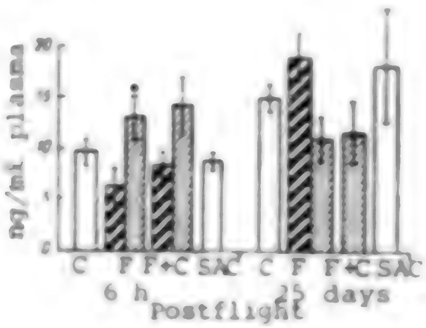

Figure 2.

E level in plasma of rats flown aboard Cosmos-936 biosatellite

Plasma E and NE levels in rats of the vivarium control were higher than CA levels in plasma of rats at rest [6, 7]. However, it should be emphasized that the low CA concentrations were demonstrated in blood taken from a rat with a special catheter introduced in an artery, and decapitation itself increases CA content of plasma by several times [7]. The rats in the Cosmos-936 experiment were decapitated; for this reason the high CA content of blood plasma is quite understandable in these rats. That decapitation is a strong stress factor is also indicated by the fact that E content in the blood of decapitated animals was several times higher than NE, whereas the opposite is true for blood taken through a catheter. The medullary layer of the adrenals is activated very rapidly and for this reason the plasma E level is so high in decapitated animals. There was a maximum of 2-3-fold increase in NE content of plasma of flight rats. It is interesting to note that elevation of CA level did not exceed a 2-3-fold change in immobilized decapitated rats [7], whereas the increase in CA in blood taken by cannulation from the same rats was 40-80 fold [7]. Thus, considering that the animals were decapitated, we could not expect more significant changes in CA level in plasma of flight rats.

During the Cosmos-936 experiment, one of the groups of animals was exposed to AG during flight to examine the effects of weightlessness. However, plasma NE levels in both flight groups were the same and were about 2.5 times above control values. This indicates that it was not long-term weightlessness, but the influence of some other factor, to which the rats were exposed in flight with weightlessness as well as AG, or else the influence of the biosatellite landing maneuver (since the centrifuge that generated AG was turned off several hours before landing, the landing maneuver was the same for both groups), that was the cause of elevation

of NE content of plasma. At the same time, the landing maneuver, as an acute stress factor, should have also activated the medullary layer of the adrenals; however, there was only insignificant elevation of plasma E level in flight rats. Expressly the adrenal medullary layer is 95% of the E source in blood plasma under stress, while sympathetic nerve endings are 70% of the NE source. For this reason, the space flight, together with the landing maneuver, activates primarily the peripheral sympatheticus and, to a lesser extent, the medullary layer of the adrenals.

In repeatedly immobilized decapitated rats, CA level in plasma (mainly E) was reliably elevated [9]. At the same time, no elevation of E level was demonstrated in flight rats submitted to weightlessness, as compared to rats exposed to AG during the flight. These data confirm the fact that long-term exposure to weightlessness is not a stressogenic impulse for the adrenosympathetic system.

E and NE levels of flight rats did not differ from control values 25 days after landing; however, it was amazing that, expressly at this time, CA levels in plasma of rats in control groups were elevated. Our previous studies revealed that minor stress (manipulations, transportation of rats) caused an appreciable rise of plasma CA levels [7]; for this reason, the high CA level in plasma of control groups of rats sacrificed 25 days after termination of the experiment is apparently due to manipulations with these animals (for example, transportation on the day they were sacrificed).

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METHODS

UDC: 629.78:574.685]:[612.463:579.8

INFLUENCE ON UREA HYDROLYSIS OF TYPICAL MICROFLORA OF URINE AND PRESSURIZED HABITATS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 27 Jan 81) pp 84-86

[Article by T. Ye. Lebedeva, I. V. Yakimova, N. M. Nazarov and S. V. Chizhov]

[Text] Man's exposure to actual space flight conditions is associated with a number of functional changes in different systems and the body as a whole. In particular, the intensive discharge of microorganisms from the human integument into the environment in a pressure chamber increases by a factor of 10^1-10^2. This makes it necessary to continue studies of the role of microflora in the process of dissociation of urea contained in urine, since the ammonia released as a result of hydrolysis pollutes the atmosphere of the sealed space, has an adverse effect on the quality of water reclaimed from urine and complicates the regeneration process proper [1, 2].

Urine can serve as the nutrient medium for many microorganisms. It contains more than 230 chemical compounds, including mineral and organic salts, amino acids, vitamins, etc. Urea is the main nitrogen-containing component of urine, and daily excretion thereof constitutes 20-35 g [3].

There is a large group of urobacteria that can hydrolyze urea to ammonia and carbon dioxide. Thanks the the enzyme, urease, such bacteria as Sporosarcina ureae, Proteus vulgaris and Bacillus pasteurii can decompose all of the urea present in a substrate [4]. As a result, up to 20 g ammonia can be found in a 24-h batch of human urine.

Urease has been found not only in typical urobacteria, but in more than 200 species of bacteria that can also utilize urea as the source of nitrogen [5]. Of greatest interest are microorganisms that can get into the atmosphere of a confined space from urine while it is being gathered and stored.

The results of studies conducted by Soviet and foreign authors revealed that the microflora of the air atmosphere and inside surfaces of manned habitats consists chiefly of human automicroflora [6]. Microbiological studies conducted in the United States in the course of assembling and testing two Viking spacecraft revealed that microorganisms directly linked to man are encountered in the atmosphere of manned compartments in 73% of the cases, while staphylococci, streptococci, micrococci, representatives of the genera Proteus, Bacillus and Escherichia are encountered in 65-75% of the cases [7].

On the basis of these data, we selected several types of microorganisms that are typical of the human automicroflora and atmosphere of sealed chambers as the most probable representatives of microflora that contaminates urine when it is being collected and stored in the manned habitat.

Our objectives included the following: investigation of dynamics of total number of microorganisms of urine when stored for a long time under nonsterile conditions and comparison to dynamics of decomposition of urea and accumulation of ammonia in urine; determination of quantity of microorganisms and intensity of decomposition of urea when sterile urine is used for monocultures of bacteria that are the most typical of the microflora of urine and sealed habitats; comparative evaluation of urease activity of several strains of bacteria isolated from the interior surfaces of a manned spacecraft in flight and analogous stock ["museum"] strains.

Methods

We studied the dynamics of live bacterial population by culturing dilute urine on solid agar media: beef-extract agar (BAA), BAA with urea and Endo medium. We evaluated the capacity of microorganisms to utilize urea as a source of nitrogen according to decrease in level thereof in urine, increase in ammonia concentration and related change in active reaction of urine.

The material for cultures consisted of 24-h stock cultures of Proteus morganii, Pseudomonas aeruginosa, Escherichia coli, as well as strains of Proteus mirabilis, Bacillus anthracoides, Staphylococcus aureus and Staphylococcus epidermidis, which were isolated, under the supervision of Prof S. N. Zaloguyev, from the interior surfaces of the Salyut-6 station in flight and kindly furnished to us by N. D. Novikova, candidate of medical sciences.

We determined whether the tested strains could hydrolyze urea by means of comparison to urease activity of a typical urobacterium, Micrococcus ureae.

Experiments were conducted in 6-9 duplications over a period of 30 days.

Results and Discussion

This work was done in several stages. At the first stage we examined processes in nonsterile urine stored for 30 days.

Figure 1 illustrates the dynamics of total microflora population of nonsterile urine and changes in indicators of decomposition of urea. By the 6th-10th day of urine storage, the number of microorganisms increased by a factor of 10^5, after which it remained at this level throughout the experiment. However, biochemical activity of the microflora persisted to the end of the experimental period, as can be seen from the continued decrease in urea content, increase in ammonia concentration and urine pH.

At the next stage, we tested the capacity of bacterial monocultures to develop in sterile urine, using urea as the source of nitrogen.

We found that bacteria of the genera Micrococcus and Pseudomonas presented the most intensive growth and largest number. Growth of Proteus was less intensive,

spread over a longer time and the population was smaller on the average by a factor of 10^3-10^4 than the preceding forms.

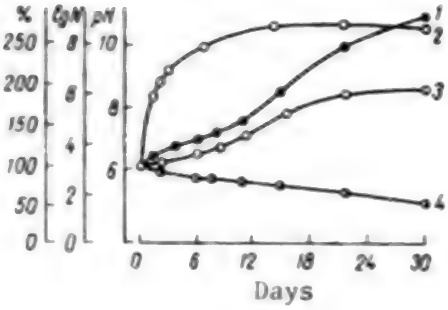

Figure 1.
Dynamics of urine microflora population size and change in parameters of urea hydrolysis
1) ammonia concentration
2) number of microorganisms
3) medium pH
4) urea content

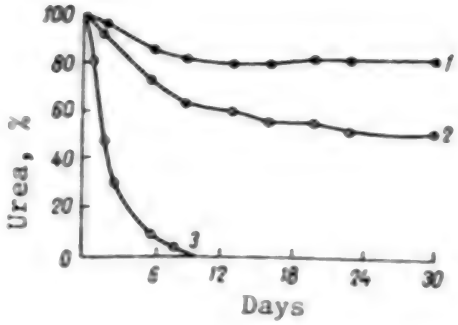

Figure 2.
Dynamics of urea content of urine under the influence of different cultures of microorganisms
1) Bacillus pyocyaneus
2) Proteus mirabilis
3) Micrococcus ureae

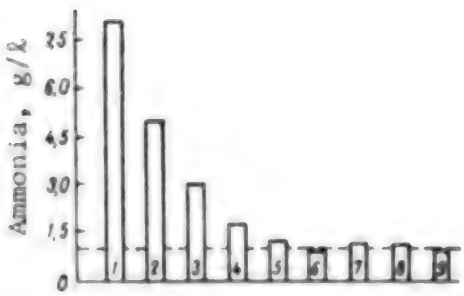

Figure 3.
Change in ammonia concentration in urine under the influence of different bacterial cultures by the 10th experimental day
1) Micrococcus ureae
2) Proteus mirabilis
3) Bacillus pyocyaneus
4) microflora of urine
5) E. coli
6) Bacillus anthracoides
7) Proteus morganii
8) Staphylococcus aureus
9) S. epidermidis
Dash line--control level

However, the biochemical activity of the tested cultures with regard to decomposition of urea did not always correspond to the population size. Thus, Figure 2 shows that the actively growing typical urobacterium, Micrococcus ureae, decomposed urea completely by the 10th experimental day. By the end of the experiment, the slow-growing Pr. mirabilis culture broke down half the existing urea, while the representative of the genus Pseudomonas, the number of which was no smaller than that of the most active bacterium, Micrococcus, decomposed only 20% of the urea.

The microorganisms were similarly distributed according to capacity to accumulate ammonia in the medium. The highest activity was inherent in Micrococcus and the lowest in Pseudomonas, Proteus occupying an intermediate position.

The dynamics of increase in pH also conformed entirely with the ammonia concentration in urine during storage.

Figure 3 illustrates ammonia concentration in urine after 10-day cultivation of monolayers of the tested microorganisms, on the basis of which we can assess their relative activity according to urea decomposition. This confirms, once more, that aside from the typical urobacterium, Micrococcus, maximum urea hydrolyzing activity was demonstrated by representatives of Proteus and Pseudomonas, whose activity can be compared to that of microflora of nonsterile urine. This is probably related to the fact that expressly Pseudomonas is one of the dominant forms of overall urine microflora, which ejects other forms of bacteria as urine storage time increases.

It is important to mention that cultures of the other tested microorganisms (such as Escherichia, Bacillus, Staphylococcus) did not manifest a capacity for hydrolysis of urea throughout the experiment.

A comparison of growth rate and ureas activity of two stock species cultures and analogous bacterial strains present in actual space flight failed to demonstrate appreciable differences. The few differences that were present were random in nature and statistically unreliable. This indicates that no irreversible changes in urease activity occur in microorganisms exposed to weightlessness for a long time, and this is important to evaluation of urine storage conditions in spacecraft.

The results of our studies revealed that, of the eight representatives of microflora of urine and habitat environment, the greatest capacity for urea hydrolysis during storage of urine is present in representatives of Proteus and Pseudomonas, in addition to typical urobacteria.

The rate of hydrolysis of urea and production of ammonia is determined primarily by the composition of microflora. Thus, in the absence of typical urobacteria, maximum ammonia content of urine by the 30th day of storage constituted 2300 mg/ℓ, which is 2.8 times more than the initial amount.

In the presence of urobacteria in urine, maximum concentration of urine ammonia increased by 10 times and constituted 8300 mg/ℓ by the 10th experimental day.

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BRIEF REPORTS

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HEMATOLOGICAL LESIONS AS A FUNCTION OF DOSAGE OF LONG-TERM RADIATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 11 Sep 79) pp 86-89

[Article by V. G. Gorlov and O. V. Neyman]

[Text] Of greatest hazard during actual space flights is the radiation from high-energy solar flares, the dose rate of which may range from under 10 to hundreds of roentgen per day [1-3]. With exposure to radiation at dose rates of the order of tens to hundreds of roentgen per day, as with acute irradiation in doses exceeding 50-100 rad, the blood changes are among the main criteria for assessing the effects of ionizing radiation on the body. There is rather complete coverage in the literature of questions of changes in the blood system related to acute radiation, as well as occupational exposure to radiation at rates of 0.02-0.1 R/day [4]. At the same time, radiobiology is only starting to gather information about the patterns of damage and recovery of the blood system as related to prolonged irradiation [5, 6].

Our objective here was to study the quantitative patterns of damage to the blood system in the course of prolonged exposure to the ionizing radiations inherent in space, as well as to determine the time characteristics of development of lesions in different blast elements. An effort was made to determine the minimal volume of hematological tests during long-term exposure to radiation to assess the general state of the blood system, on the basis of comparison of dynamics of changes in bone marrow and peripheral blood.

Methods

Experiments were conducted on 285 mongrel rats weighing 180-200 g. The animals were exposed to radiation at dose rates of 300, 100 and 50 R/day. They were exposed continuosuly for 22-23/day. With accretion of cumulative doses of the order of 30-2700 R, we assessed hemopoiesis according to cell composition of bone marrow and peripheral blood parameters. We used seven animals for each experimental point.

Results and Discussion

Analysis of our findings revealed that the dynamics of decline in total number of bone marrow cells during the phase of primary depletion (Figure 1a) is governed by an exponential law. There was distinct demonstration of the effects of cumulative dose and dose rate. However, there was subsequent prevalence of the effect of

dose rate. A typical finding in all cell populations of bone marrow was an initial exponential decline in number of cells. Depending on the radiation dose rate, erythroblast elements of bone marrow (Figure 1b) was either stabilized on a specific level (50 R/day), or else, after reaching a maximum lesion they gradually recovered to 70-80% of the control (100 R/day). With a dose rate of 300 R/day, there was a period of brief increase in erythronormoblasts followed by a second decrease. The dose-effect curves for myeloid cells were exponential over the entire period of irradiation, there being an initial "arm" in the region of radiation doses of 30-150 rad (Figure 1c).

The nature of changes in lymphoid elements of bone marrow was related to radiation dose and dose rage (Figure 1d). After a sharp decline in number of lymphoid elements with delivery of 30-300 rad, we observed a period of stabilization of their number in bone marrow, the level and duration of which were determined essentially by the radiation dose rate.

The results of our tests revealed that the reticular cells of bone marrow as a whole are notable for a high degree of radiosensitivity (Figure 1e). Thus, with delivery of radiation at dose rates of 50 and 300 R/day, 50 rad was the dosage that led to 50% cell death. The rapid decline in number of reticular stromal cells, which was inherent in the first stage of irradiation, was followed by a rise in their number. With increase in irradiation time (50 R/day), there was relative stabilization of reticular cell content of bone marrow. With the use of 300 R/day, we demonstrated a period of secondary decline in number of stormal elements and a new recovery phase. The curve of dynamics of these cells with irradiation at a dose rate of 100 R/day presented segments of exponential decline and relative stabilization on a level of 25-30%, as compared to the control.

On the whole, the findings in peripheral blood during long-term irradiation were similar to the changes observed in bone marrow. There were, however, some differences in the patterns of radiation damage to bone marrow elements and peripheral blood, which we should mention in order to try to establish the time correlations between dynamics of changes therein. The greatest analogy of dynamics of changes in bone marrow and peripheral blood is apparent when we compare such hemopoietic parameters as quantity of bone marrow cells or myeloid cell content, as well as quantity of neutrophils and total leukocytes in peripheral blood (Figure 2a, b). More substantial differences were found upon comparing the quantitative characteristics of myelokaryocytes and lymphocytes of blood (Figure 2c). While the nature of damage to the pool of lymphoid elements in bone marrow and all lymphoid tissues of the organism delivering lymphocytes to peripheral blood (and, perhaps, bone marrow) was the same, we must mention the presence of considerable differences in dynamics of changes in quantity of lymphoid elements in bone marrow and peripheral blood. Accordingly, we can foresee some inaccuracy in assessing bone marrow hemopoiesis on the basis of quantity of lymphocytes. At the same time, the independence of degree of damage to lymphopoiesis from dose rate, which we demonstrated (see Figure 2c) with cumulative doses of 30-250 rad, is indicative of the informativeness of such a parameter as lymphocyte content of peirpheral blood for determination of damage to the hemopoietic system.

Erythrocyte content in the course of prolonged irradiation did not reflect the extent of damage to the bone marrow's erythropoietic system (Figure 2e). Because of the long life span of mature erythrocytes (weeks or even months) and relatively insignificant reduction of their lifetime during prolonged irradiation [7], extensive

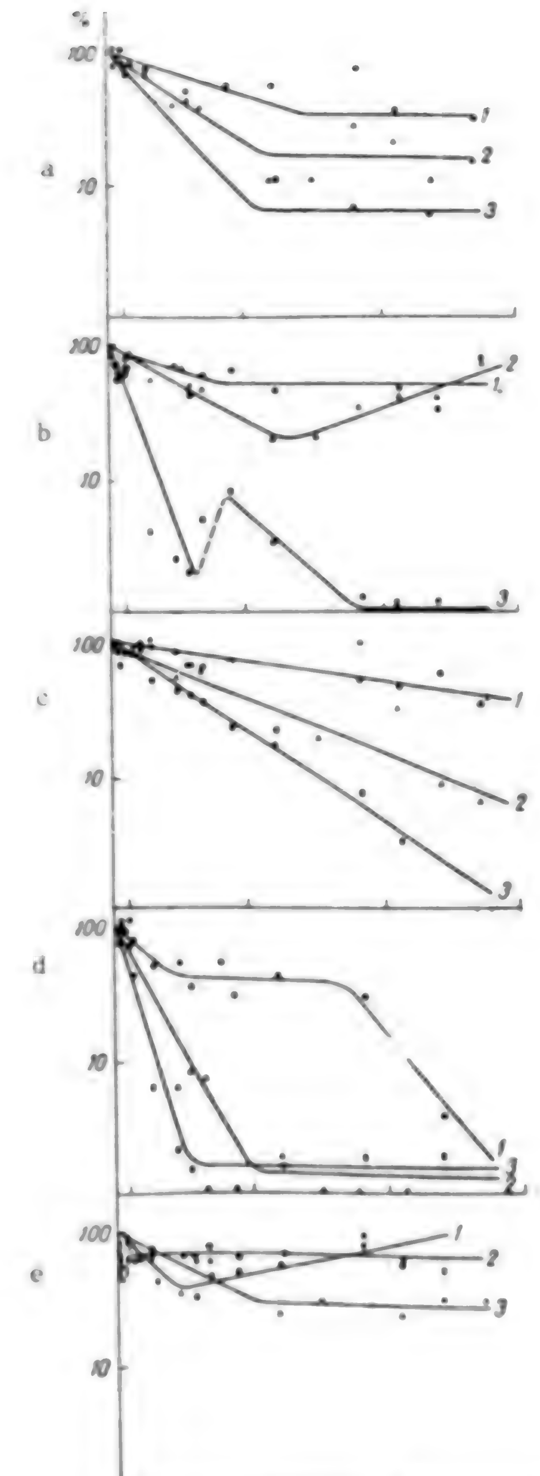

Figure 1.
Rat bone marrow parameters with irradiation at dose rates of 50 (1), 100 (2) and 300 (3) R/day (% of control)

a) myelokaryocytes
b) erythroblast elements
c) granulocyte elements
d) lymphoid elements
e) reticular cells

experimental studies will be needed in order to determine the relationship between manifestations of postradiation anemia and radiation dose rate. At the present time, it can only be maintained that it is difficult to predict in the short term the sequelae of damage to the erythropoietic system on the basis of severity and speed with which anemia develops during long-term exposure to radiation.

Analysis of development of damage to thrombopoiesis revealed phasic dynamics (Figure 2d). During the first day of irradiation there was appreciable (10-75%) decrease in number of platelets. At subsequent times, there may be some increase in their number (100 R/day) or stabilization of thrombocyte count on a level that is more or less lower than in the control (300 R/day). Thereafter the curves of decline in number of thrombocytes are described satisfactorily by an exponential function. All this indicates that the thrombocyte content of blood is one of the most sensitive tests for evaluating effects of long-term irradiation.

The Table lists doses leading to 50% decline in number of cells of different generations and, accordingly, the time periods of manifestation of this effect, which were calculated for exponential segments of dose-effect curves. As in the case of brief exposure to acute radiation, the different cellular elements of the blood system different in sensitivity to prolonged irradiation. Lymphoid elements of bone marrow, peripheral blood lymphocytes and erythroid cells of bone marrow were the most radiosensitive. They were followed, in order of ascending doses leading to 50% death of cells, by leukocytes, bone marrow cells, neutrophils and myeloblast elements.

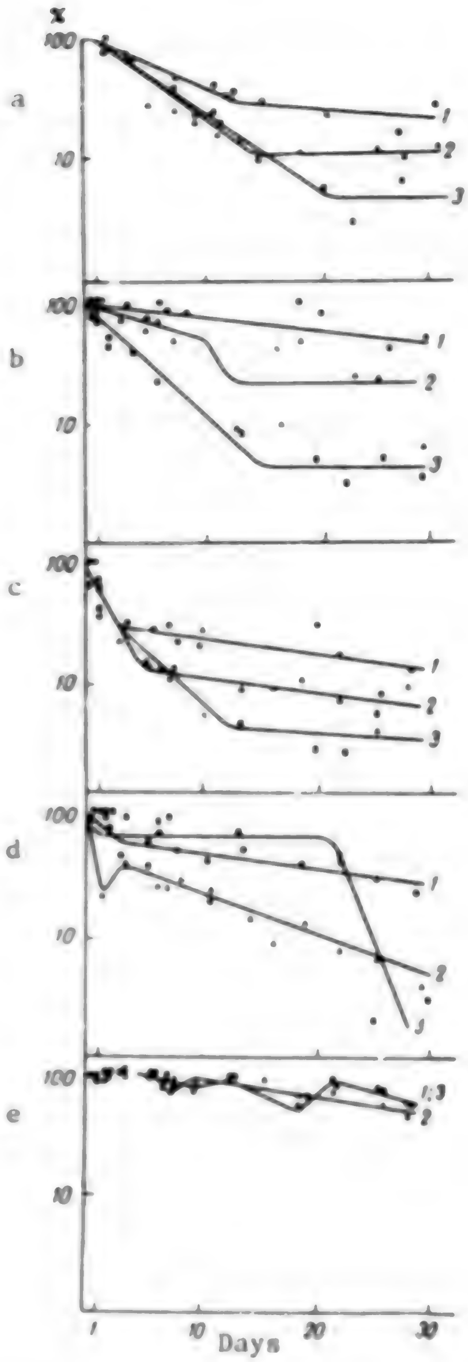

Figure 2.
Parameters of rat blood with irradiation at dose rates of 50 (1), 100 (2) and 300 (3) R/day
a) leukocytes
b) neutrophils
c) lymphocytes
d) thrombocytes
e) erythrocytes

Thus, the dose-effect curves indicate that virtually all populations of hemopoietic cells are heterogeneous in radiosensitivity. The initial exponential decline in the most radiosensitive cells, which is apparently the result of loss of cellular reproductive function, their interphase death and natural loss of intact functional cells, could be an important diagnostic sign of severity of radiation lesion due to prolonged exposure to radiation. During exposure to radiation, as a result of selection of resistant cells [8] in the hemopoietic system, a period of dynamic equilibrium between processes of damage and recovery appears, and the intensity thereof is determined primarily by the radiation dose rate. The duration of this period also depends on intensity of radiation. There is reason to believe that there are interspecific differences in time of appearance and duration of these reactions in different cell populations of hemopoietic tissue [9]. Hence the difficulties involved in extrapolating the obtained data to man. At the same time, there were negligible differences in the early reaction of the blood system of most animals studied by different authors [10]..

The damage to the hemopoietic system from extended irradiation is just as inevitable an effect of ionizing radiation as in the case of acute radiation sickness, the only difference being that prolonged irradiation is characterized by a slower rate and lesser degree of damage, as compared to acute irradiation in the same dosage. According to the Table, 50% death of different hemopoietic cells exposed at a dose rate of 300 R/day occurred in 0.3-1.5 days, which corresponds to the time of development radiation damage to the hemopoietic system following acute irradiation [11, 12]. With decrease of dose rate to 100 R/day, 50% death occurred at 1.5-7.0 days for different cellular elements and at 50 R/day at 3-50 days. According to the data in [13-15], the time of 50% death of blood cells (leukocytes) constituted 50-200 days in mice, rats, guinea pigs, rabbits and dogs with reduction of dose rate to 0.5-10 R/day.

Radiosensitivity of different cellular elements of hemopoietic system with prolonged exposure to radiation

Cellular elements	Dose leading to 50% death of cells, R/day			Half-life of cells (days) with doses, R/day		
	300	100	50	300	100	50
Myelokaryocytes	230	450	930	0.9	4.5	18.6
Leukoblast elements	460	700	2700	1.5	7.0	54
Erythroblast "	120	530	800	0.4	5.3	16
Lymphoid "	100	170	350	0.3	1.7	7
Leukocytes	250	220	460	0.8	2.2	9.2
Neutrophils	330	1000	2550	1.1	10	51
Lymphocytes	150	150	150	0.5	1.5	3.0
Thrombocytes	35*	20*	100*	0.1	0.2	2
Reticular cells	50	—	50	0.16	—	0.5

*80% loss of cells.

The rate of build-up of damage to hemopoiesis is demonstrable the most distinctly by counting lymphocytes, total leukocytes, thrombocytes of peripheral blood, lymphoid elements, erythronormoblasts and total cells of bone marrow. We can judge primarily the severity and time of development of damage to hemopoiesis during long-term exposure to radiation on the basis of data on radiosensitivity of expressly these cellular elements and dynamic studies of the rate of decline thereof in the different cell pools. Such validations are meaningful only when solving the problem of setting the optimum minimum of hematological monitoring in the case of extended irradiation. Of course, the rate of damage to the hemopoietic system as a whole is determined by the rates of depletion of all its components. However, by establishing the time correlations between rates of depletion of bone marrow and of decrease in quantity of lymphocytes, neutrophils and thrombocytes, one can predict the state of bone marrow hemopoiesis at a given point in time in the course of prolonged exposure to radiation.

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SEROTONIN AND HISTAMINE METABOLISM IN COSMONAUTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 (manuscript received 21 Feb 80) pp 89-91

[Article by Z. S. Dolgun, S. A. Meshcheryakova, M. S. Belakovskiy and V. I. Legen'kov]

[Text] Serotonin (S) and histamine (H) concentration in animal and human blood, as well as excretion of 5-hydroxyindoleacetic acid (HIA) in urine, change under cold stress and high temperatures [1], anaphylactic shock [2], hypoxia [3], short- and long-term vibration, the influence of pulsed noise and combined effect of these factors [4], during prolonged hypokinesia. Certain changes were demonstrated in blood S content in animals examined after returning from a short-term space flight [6, 7].

In view of the role of S and H in regulating metabolic processes, it is interesting to obtain information about the metabolism of these substances in cosmonauts. Our objective here was to examine the effects of preflight training [preparations] and space flight conditions on some parameters of S and H metabolism in man.

Methods

Venous blood and 24-h urine served as the material for our studies.

We assessed S metabolism according to 24-h excretion of its precursor--tryptophan (T), product of its intermediate metabolism--5-hydroxytryptophan (HTR), S proper and one of the main products of its inactivation--HIA, as well as according to levels of these compounds in venous blood. We examined H metabolism following the same scheme, i.e., according to excretion of H and its precursor--histidine (HD) and according to levels of these compounds in venous blood.

Blood was taken from the ulnear vein on a fasting stomach between 0800 and 0900 hours. The compounds studied were isolated from blood and urine on columns with Dowex 50-mesh ion exchange resin. We assayed the isolated compounds by fluorometry [8]. The findings (see Table) were submitted to statistical processing, using the criterion of Fisher-Student [9]. The range of normal values was taken from [8].

We examined 4 groups of clinically healthy men 25 to 40 years of age. The first (control, 27 men) group consisted of subjects who had undergone a course of special

training before enrolling in the cosmonaut detachment; the second group (12 men) consisted of cosmonauts who had participated in one space flight previously; the third (8 men) consisted of cosmonauts who had flown in space twice; the fourth consisted of individuals who had not undergone any special training (42 people). From 2 to 4 years had elapsed between completion of the flights and time of these studies.

T, HTR, S, HIA, HD and H levels in human blood and urine

Group	Tested material	Number of subjects	Levels in blood (μM/ℓ) and urine (μM/day)					
			T	HTR	S	HIA	HD	H
1	Blood	19	66.30±5.62	1.27±0.19	1.50±0.11	2.24±0.20	194.5±35.16	2.78±0.30
	Urine	27	202.15±16.9	2.63±0.51	1.59±0.15	6.43±1.31	592.8±191.37	3.06±0.29
2	Blood	6	87.53±17.60	1.36±0.26	1.64±0.19	1.62±0.26	142.19±29.5	3.05±0.26
	Urine	12	96.40±7.57	1.63±0.18	1.30±0.11	8.00±1.67	767.97±247.9	2.69±0.26
3	Blood	5	164.65±40.39	1.77±0.06	1.24±0.15	3.39±0.73	166.0±28.72	3.32±1.11
	Urine	8	160.78±31.93	2.00±0.56	1.58±0.31	10.46±1.51	634.98±248.3	2.69±0.98
4	Blood	30	54.91±2.98	0.40±0.03	1.36±0.06	0.50±0.03	197.58±0.57	0.99±0.01
	Urine	42	96.82±8.50	1.49±0.09	0.79±0.11	14.22±1.04	1701.45±211.9	0.89±0.17
Normal range	Blood		29—120.5	0—0.18	0.34—1.00	0—0.7	31.6—451	0.23—1.2
	Urine		48.5—196	0.93—7.1	0.77—1.7	9.4—23.5	120—3198	0.13—1.2

Results and Discussion

On the average, blood T content was higher in the 3d group of subjects than the 4th, as well as 1st and 2d groups. HTR level was also higher in this group of subjects, constituting 107, 130 and 433% of the parameters of subjects in the 1st, 2d and 4th groups, respectively. S concentration was virtually the same in all groups, whereas HIA was highest in the 3d group, constituting 151, 210 and 477% of the levels for subjects in the 1st, 2d and 4th groups, respectively.

Total H in the blood of subjects in the 1st, 2d and 3d groups was higher than in the 4th. However, this did not lead to any clinical manifestations of hyperhistaminemia. In all likelihood, this could be attributed to the high histaminopectic activity of blood protein, which reduces the amount of free H with biological activity and could play a pathogenic role. The increase in total H content of blood is apparently due to increase in its bound forms, which do not have biological activity, which are a reserve and could provide at any time the required amount of free H.

In view of the fact that a single assay of the above parameters in blood in the morning cannot provide complete information about their metabolism in the course of the day, we analyzed these compounds in 24-h urine.

The subjects in the 1st group presented a reliable increase in daily excretion of T, as compared to parameters of the 2d and 4th groups ($P<0.05$). HTR content in 24-h urine was higher in subjects of the 1st group than the other groups. Excretion of S was the same in cosmonauts of the 2d and 3d groups as in the 1st group, but was double the mean level for subjects in the 4th group. Daily excretion of HIA was increased in subjects of the 2d and particularly 3d groups, as compared to the 1st ($P<0.05$), but less than in the 4th group.

Thus, assays of parameters of S metabolism in blood and 24-h urine revealed differences chiefly in T and HTR, the levels of which in blood were elevated in the 2d and 3d groups of subjects and in urine, in the 1st group. HIA level in urine was higher in the 2d and 3d groups than the 1st. The explanation for this finding should apparently be sought in the change in intensity of S metabolism over a 24-h period. It can be assumed that production of S, associated with utilization of T and HTR, in the mornings occurred more intensively in subjects of the 1st group than the 2d and 3d. On the whole, there was more active metabolism of S in the 2d and 3d groups of subjects over a 24-h period than in the 1st group, which is indicated by lower T and HTR levels in 24-h urine of subjects in the 2d and 3d groups and higher level of HIA excretion.

Daily excretion of H was increased in the first 3 groups, as compared to the 4th, whereas HD excretion was significantly lower. The latter may be indicative of increased synthesis and elimination of H in subjects of the first 3 groups.

Thus, the subjects in the 2d and 3d groups demonstrated an increase in intensity of S metabolism, synthesis thereof, as well as processes of its biological inactivation, as compared to the parameters for the 1st group. These changes were the most marked in the 3d group of cosmonauts. The higher functional level of this system is apparently one of the manifestations of cosmonauts' adaptation to space flight factors.

Concurrently, we demonstrated an increase in overall H content due to synthesis thereof in the 1st-3d groups of subjects, as compared to the 4th group.

The results of assaying the above compounds in blood and excretion over a 24-h period are consistent with data in the literature.

In view of the fact that our findings were obtained on an insignificant number of subjects, we consider them to be preliminary. Work in this direction will be continued.

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CURRENT EVENTS AND INFORMATION

UDC: 612.014.4:061.3(47+57)"1980"

FIRST ALL-UNION SYMPOSIUM ON 'PROBLEMS OF EVALUATING AND FORECASTING MAN'S FUNCTIONAL STATES IN APPLIED PHYSIOLOGY'

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 pp 91-92

[Article by A. A. Maksimov]

[Text] The First All-Union Symposium on "Problems of Evaluating and Forecasting Man's Functional States in Applied Physiology" convened in Frunze on 29 September to 1 October 1980. This symposium was organized by the Scientific Council for Complex Problems of Human and Animal Physiology, USSR Academy of Sciences, and Institute of Physiology and Experimental Pathology of High Altitudes, Kirghiz Academy of Sciences.

At the symposium, papers on the following topics were delivered: forecasting man's functional state in aviation and cosmonautics; forecasting man's functional state during exposure to various environmental factors; forecasting the functional state of athletes; forecasting the functional state of the body in industrial physiology; forecasting in human ecology; reliability of man-machine systems.

The problem of predicting man's functional states, his health and work capacity arose the most acutely before worldwide science in the last 20 years, because of the rapidly changing working conditions in many sectors of the national economy, development of new industrial territories and inhabited regions, space flights, exploration of the shelf and depths of the world oceans. Many millions of people live and work under unusual environmental conditions, often with very extreme ambient factors. It must be noted that the Soviet public health system has been called upon to play a special role in forecasting, since it has proclaimed that its guiding principle is prophylaxis and prevention of diseases, pathological states, loss of work capacity or decline thereof. In this aspect, the goals and tasks of Soviet public health and medical forecasting are the closest. Biomedical forecasting not only aids in developing the scientific theoretical base for a set of preventive measures, but solves a number of other practical problems, starting with medical and professional screening of specialist groups, ending with elaboration of a set of sociobiological and medical measures to preserve a high level of work capacity and human health under extreme living conditions.

Many aspects of these problems were the subject of discussion at the symposium. More than 150 people (including 107 doctors and candidates of sciences) from 32 different cities of our homeland participated in the symposium sessions.

There were plenary and section meetings for 3 days. The papers dealt with general theoretical and methodological aspects of forecasting and evaluating man's functional states; they offered a general description of the level of development of the problem, outlined the routes and prospects of future research on the problem of prognostic studies in applied physiology.

Several decisions were adopted at the symposium, consisting of the following.

It was deemed mandatory to further develop work on complex research in the area of biomedical forecasting with broad involvement not only of scientific research institutes and organizations, but medical VUZ's and practical public health institutions.

It was recommended that research be expanded with regard to defining the most informative prognostic criteria, that could be introduced into practice on a broad scale, for evaluating the functional states of sick and healthy man in order to develop standardized recommendations on screening people for work under special conditions. It is expedient to recommend the use of forecasting methods for evaluating the health status of the public through mass scale preventive examinations, in scientific organization of labor, theory and practice of physical education and sports in order to set objective standards of work loads and working conditions, as well as to provide for optimum interaction between man and machines.

Noting the important role of biomedical forecasting in solving theoretical and practical problems of biological and medical science, it is deemed desirable to include, in the teaching system at biological and medical VUZ's, optional lecture cycles on forecasting physiological states. For the practical implementation of these tasks, the appropriate initiative working group should be formed within the framework of the Scientific Council for Complex Studies of Man under the USSR Academy of Sciences.

The organizational and scientific activities of the Institute of Physiology and Experimental Pathology of High Altitudes, Kirghiz Academy of Sciences, are to be commended in the area of organizing the First All-Union Symposium on Forecasting in Applied Physiology and for establishing productive scientific contacts with concerned institutions of the USSR Academy of Sciences, USSR Academy of Medical Sciences, USSR Ministry of Higher Educational Establishments and USSR Ministry of Health.

It is deemed expedient to establish new departments (laboratories, groups) at scientific research institutes for operational handling of scientific and practical problems of public health and the national economy, in order to intensity and concentrate scientific research dealing with the problem of evaluating and forecasting man's functional states under extreme environmental conditions.

It is deemed necessary to draw the attention of wide circles of researchers to theoretical and practical problems of forecasting in human ecology.

It was deemed expedient to convoke a symposium dealing with problems of biomedical forecasting once every 3 years.

The next symposium (conference) is to be held in Frunze in 1983.

SEVENTH ALL-UNION SCIENTIFIC CONFERENCE ON SPACE BIOLOGY AND AEROSPACE MEDICINE SCHEDULED

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 p 92

[Announcement by editorial board]

[Text] In accordance with the plan for holding All-Union scientific conferences, meetings and congresses, the Organizing Committee for the 7th All-Union Scientific Conference on Space Biology and Aerospace Medicine announces that this conference will convene in Kaluga on 23-25 June 1982.

The conference will be held under the slogan of "Achievements of space biology and aerospace medicine for practical applications."

At the same time, there will be a conference of readers of the journal, "Kosmicheskaya biologiya i aviakosmicheskaya meditsina" [SPACE BIOLOGY AND AEROSPACE MEDICINE].

BOOK REVIEWS

UDC: 612.886+616.282](049.32)

NEW BOOK DEALS WITH CLINICAL NEUROPHYSIOLOGY OF THE VESTIBULAR SYSTEM

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 pp 92-93

[Review by V. A. Kislyakov and M. M. Levashov of book "Clinical Neurophysiology of the Vestibular System" by R. W. Baloh and V. Honrubia, in "Contemporary Neurology Series," 18, F. A. Company, Philadelphia, 1979, 230 pages]

[Text] The names of the authors of the monograph being reviewed are well-known to Soviet specialists--labyrinthologists, otoneurologists and physiologists--from their works published in the last 10 years dealing with clinical neurophysiology of vestibular and hearing functions, in particular differential diagnostics based on quantitative analysis of oculomotor reactions in different tests: vestibular and optokinetic nystagmus, tracking eye movements, pathological forms of nystagmus, etc. These studies have been reflected in the monograph, with organic integration with analysis of extensive literature dealing with clinical neurophysiology of the vestibular systems. The authors succeeded in selecting from the profusion of literature what could be of direct interest to a practical clinician, omitting from the book all debatable issues or those that have not yet found practical confirmation.

The monograph consists of seven chapters, the first three of which deal with a laconic description of the fundamentals of anatomy and physiology of the central and peripheral parts of the vestibular system.

The first chapter is in the nature of an expanded introduction, which touches upon general questions of biophysics and morphology of receptors, classification of vestibular reflexes, organization of central pathways, phylogenesis of the vestibular system, etc.

The second chapter deals entirely with the peripheral part of the vestibular system. It submits information on functional anatomy of the labyrinth, its blood supply and innervation. The presentation is made in a simple form and to the extent required by a practicing clinician. The semicircular canals and otolith organs, mechanisms of their stimulation, as well as features of primary afferentation elements, are described.

The third chapter covers a wide range of questions pertaining to the central regions of the vestibular system. It describes vestibular nuclei--their morphology, physiology, connections and interaction. A significant place is devoted to a description of vestibular and oculomotor reflexes, methods of testing them,

mechanisms of organization of reflexes from semicircular canals and otolith organs. The characteristics of eye movements elicited by stimulation of receptors of the semicircular canals are given. Special attention is devoted to nystagmus--its mechanisms, effect on it of eliminating different elements of the system and extinction. There is discussion of otolith reflexes, interaction between reflexes of semicircular canals and otolith receptors, as well as visual and vestibular interaction, anatomical and physiological bases. Importance is attributed to vestibulospinal reflexes, the pathways over which they interact with the cerebellum and postural control. The chapter ends with a description of vestibulosensory reflexes--anatomy and physiology of vestibular sensations, psychophysics and motion sickness.

These three chapters are the foundation, upon which the rest of the monograph, which is directly referable to clinical practice, is constructed.

The fourth chapter is concerned with clinical examination in the presence of vestibular dysfunctions: analysis of history and complaints, determination of prior factors, patient examination, testing posture, pathological forms of nystagmus (spontaneous, vestibular, positional, fixation, etc.). The good diagrams and tables submitted in this chapter help systematize the extensive material in order to make use of the information given for differential diagnostication.

Electronystagmography, being the most important area of modern vestibulometric diagnostics, is the subject of a special chapter, the fifth. In this chapter, there is reflection of the current level of development of applied tests in the area of oculomotor reactions. The significance to a clinician of evoked vestibular nystagmus, spontaneous nystagmus, optokinetic nystagmus and other eye movements, saccadic and tracking movements is demonstrated. The sections contained in this chapter are constructed on the principle of comparing the phenomena observed in the presence of pathology to the norm, whose range is defined rather clearly.

Chapter 6 contains information about clinical testing of hearing. The need for such a chapter is obvious, since a differential diagnosis would hardly be possible without comparing vestibular and audiological symptoms. The seventh chapter deals with audiological symptoms and describes the syndromes present with different levels of damage and different etiology. A description is offered of the sets of symptoms inherent in lesions to the labyrinth and endings of the eighth nerve, vestibular ganglion and nerve trunk the canal, pons-cerebellar angle, brain stem and cerebellum, and cortical projections. At the end of this chapter there is discussion of problems of etiology of vestibular disturbances, and among the etiological factors infection, vascular disturbances, tumors, trauma, metabolic disorders, etc., are discussed. Meuniere's, Cogan's syndromes, cupulolithiasis, vestibular neuronitis and others are classified among syndromes of unknown origin or with multiple etiology.

A bibliography that is proportionate to the size of the chapter (the longest one lists 350 items) accompanies each chapter, and there are minimal repetitions, although they would seem to be inevitable with such a procedure. The structure of the book is such that any of its chapters, while having independent significance, is at the same time a logical continuation of the preceding ones. It is easy to get one's bearings in the book thanks to a comprehensive subject index. The summary tables furnished in several chapters are very good and convenient: types of

pathological nystagmus, interpretation of results of bithermal test, tests of visual control, symptoms of system lesions on different levels, etc. Such tables are a good aid as a guide on results of clinical examinations. The characteristics of optical reflexes induced by stimulation of otolith systems (bending the head, acceleration, rocking on parallel swing) are described, and there is discussion of some aspects of correlations between otolith reflexes and nystagmus.

The book is well-illustrated. It is written clearly, in a simple language and it will be useful to any reader concerned with this subject: for a student this work will be an excellent textbook and for the specialist it will serve as a practical survey-manual, which sums up the current status of this branch of science and helps in getting acquainted with an extensive bibliography.

The monograph will also be useful to specialists in aviation and space medicine. First of all, it has a good physiological section, provides concrete figures characterizing the norm for various vestibulometric tests, whereas for analysis of deviations induced by extreme conditions, one can use some analogies to clinical practice which serves, as we know, as a rich arsenal of distinctive "models," and this book will help to make use of it.

UDC: 612.014.477-063(049.32)

NEW BOOK DEALS WITH GRAVITATIONAL PHYSIOLOGY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 pp 94-95

[Review by V. Ye. Katkov of book "Gravitatsionnaya fiziologiya. Seriya 'Uspekhi fiziologicheskikh nauk'. Materialy 28-go Mezhdunarodnogo kongressa fiziologicheskikh nauk" (Gravitational Physiology. "Advances in Physiological Sciences" Series, Proceedings of 28th International Congress of Physiological Sciences), edited by J. Hideg and O. Gazenko, Pergamon Press and Hungarian Academy of Sciences Publishing House, Budapest, Vol 19, 1980, 316 pages, 134 figures, 37 tables]

[Text] The proceedings of the Second Symposium on Gravitational Physiology are published in this book; this is a rapidly developing branch of physiology that deals with the mechanisms of interaction between highly organized living systems and altered gravity fields. The symposium convened during the 28th International Congress of Physiological Sciences, which was held in Budapest from 13 to 19 July 1980. Prominent specialists from many European countries and the United States participated in the symposium.

A total of 53 papers were delivered at the symposium, which are published in the book in the following sections: 1. General problems. Adaptation to altered gravity. 2. Physiological systems: metabolic and morphological studies. 3. Structure and function of gravity-sensitive systems: vestibular system, bones and muscles. 4. Hypokinesia and immobilization. In addition, in the "Miscellaneous" section there are data on vibration, decompression, heat regulation in an altered gravity field and others. It must be mentioned that the proceedings of this symposium were also published as an appendix to the journal, PHYSIOLOGIST, Vol 23, Suppl No 6, 1980.

Most papers were concerned with the results of research conducted aboard Soviet biosatellites of the Cosmos series. Special attention was given to the study of physiological effects of weightlessness simulated on the ground (antiorthostatic [head tilted down] position, hypokinesia, immobilization, etc.), which is a mandatory prerequisite for more comprehensive studies of the mechanisms of adaptation to this factor.

Bjurstedt dwelled on the history of development of gravitational physiology, told about the foundation of the Commission for Gravitational Physiology within the framework of the International Union of Physiological Sciences (IUPS) and its activities at the present time, making special mention of the importance of

cooperation of different countries to solve the pressing problems in this branch of biological science. In the next few years, specialists will concentrate, as before, on gravity-related changes in the cardiovascular system (primarily the low-pressure system), their relation to fluid-electrolyte metabolism and renal function, function of sensory organs, study of the causes of muscular atrophy and decalcification of bone tissue during long-term exposure to weightlessness, etc. The rapid development of this area makes it necessary to have new ideas and methodological procedures that would permit a more sophisticated study of the effects of gravity on highly organized living systems and, first of all, man. Such an approach would make it possible not only to study the mechanisms of adaptation to altered gravity, but some basic problems of general physiology and pathology of man.

The authors conducted a considerable amount of research using modern histological, histobiochemical and biochemical methods to study the effects of space flight factors (primarily weightlessness) on various rat organs and tissues. It was shown (and this is of basic importance) that while relatively long-term exposure of animals to weightlessness is associated with changes in a number of parameters, these changes are not necessarily pathological, and the changes observed in some tissues may be reversible. As validly noted by the researchers, the obtained results are not only necessary to comprehend the general biological patterns of adaptation to weightlessness, but have applied significance, since they make it possible to undertake development of new criteria and functional diagnostic methods, as well as medical support of manned space flights; they will also aid in forming promising directions of research in the future.

The morphological and biochemical changes observed in animals following flights aboard biosatellites of the Cosmos series are being linked by authors chiefly to the effect of weightlessness per se and the stress reaction observed during powered flight. Various morphological changes occur under the influence of weightlessness in the myocardium and skeletal muscles, bone and lymphoid tissue. Unfortunately, there has not been sufficient coverage of changes that occur in smooth muscle elements of peripheral vessels, which react immediately to changes in the circulatory gravity factor (hydrostatic component of arterial pressure). In the papers, there was analysis of the numerous parameters of protein, carbohydrate, electrolyte, oxidative and other forms of metabolism, changes in a considerable part of which could be related to the stress reaction upon returning to earth.

Also of great interest is the fact that these studies demonstrated for the first time that it is possible to use artificial gravity (AG) to prevent undesirable changes due to weightlessness. However, it should be noted that the use of AG did not always prevent onset of these changes (in particular, in the myocardium).

On the basis of flight data and results of ground-based studies, Cogoli expounded the hypothesis that there is a correlation between lymphocyte activity and G level, which could be of substantial significance to evaluation of the effectiveness of specific immune systems during and after space flights. Apparently, research in this direction will be continued aboard the Spacelab orbital station.

Significant attention was given at the symposium to the changes occurring in the bone and muscle system in weightlessness and with immobilization. Most papers dealing with this problem were delivered by Hungarian and Soviet researchers. The

publication of these papers in a single book offers an opportunity for becoming acquainted with both structural-functional and biochemical changes that occur in this system under the influence of hypogravity. The authors demonstrated convincingly that the mass and controlling properties of muscles diminish significantly under such conditions. This is one of the most important causes of demineralization of bone tissue, not only of the limbs but spine, and the degree of decalcification of different parts of the latter is not the same. It should be noted that these processes refer not only to bones with antigravity function, but those that do not directly participate in this function (for example, the mandible).

There were interesting but few papers concerned with function of the vestibular system. A number of methods (labyrinthectomy, filling with neutral mass to prevent movement of endolymph and others) were used, followed by exposure to accelerations, to investigate its role in compensation of gravity load and interaction with other systems (respiration and circulation). In addition, there was discussion of the important question of Ca^{2+} metabolism in otoliths, and its dependence on K^+/Na^+ ratio in ambient fluid was demonstrated.

As before, the specialists focused on problems of simulating the effects of weightlessness on the ground. In the opinion of Moore-Ede et al., in addition to the usual procedures (antiorthostatic position, immobilization, immersion), one can use for this purpose lower body negative pressure, which leads to an increase in central blood volume and central venous pressure. Studies of fluid-electrolyte and hormone metabolism under such conditions in monkeys revealed that some of the changes resembled those observed during the first hours of weightlessness.

Postural tests have gained the widest popularity for the study of effects of gravity factors on man. The researchers were concerned with the correlation between respiratory and circulatory control in orthostatic position, using tests with breathing mixtures containing different amounts of carbon dioxide. A method based on the Doppler effect was used to measure blood flow during gravity tests. With this method, Loeppky et al. were the first to succeed in measuring the linear blood flow rate in the crural artery during use of lower body negative pressure, while Wojtkowiak demonstrated its informativeness in assessing resistance to $+G_z$ accelerations. The method of noninvasive transcutaneous oxymetry, which can also be used during space flights, appears to be also promising for the study of gravity factors and determination of efficacy of means of preventing the adverse effects of weightlessness.

In conclusion, it should be noted that the proceedings of this symposium, which reflect rather fully the different directions of research in gravitational physiology, are indicative of rapid development of these extremely important direction and of close collaboration among scientists of different countries in such research. This book will be of interest to specialists concerned with space biology and medicine (biochemists, morphologists, physiologists, physicians), as well as other researchers working in the field of gravitational physiology.

UDC: 614.2:92(Burnazyan)

OBITUARY OF AVETIK IGNAT'YEVICH BURNAZYAN (1906-1981)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 1, Jan-Feb 82 p 96

[Article by editorial board]

[Text] Avetik Ignat'yevich Burnazyan, outstanding public health organizer, communist, Hero of Socialist Labor, recipient of the Leningrad and USSR State prizes, deputy USSR minister of health, passed away on 15 October 1981.

A. I. Brunazyan devoted his entire conscious life to selfless service to his socialist homeland, to the cause of the communist party.

A. I. Burnazyan was born on 7 April 1906 in the city of Kamo, Armenian SSR. After graduating from the Military Medical Academy, he was assigned as junior physician and traveled a glorious road up to Lieutenant General in the Medical Service. He was in the active army in the post of head of the military health directorates from the first to the last day of the Great Patriotic War. During the period of the war with Japan, he headed the military health directorate of the Second Far East Front.

A. I. Burnazyan worked at the USSR Ministry of Health from 1947 on as head of a number of administrations, and for 25 years he was the deputy minister. He made a significant contribution to the matter of organizing medical care for the nation's population and participated actively in the conception and development of space medicine.

A. I. Burnazyan, who was gifted in many areas, devoted many years of his life to scientific and pedagogic work, to the education of young physicians.

For his great services to the homeland, the title of Hero of Socialist Labor was bestowed upon A. I. Burnazyan. He was awarded six Orders of Lenin, the Order of the October Revolution, three Orders of the Red Banner of Labor, first-class orders of the Great Patriotic War, "Honor Badge" Order and many medals of the Soviet Union.

We have lost a remarkable physician and public health figure, a considerate and responsible comrade. The bright memory of this loyal son of the Communist Party,

ardent patriot of our homeland--Avetik Ignat'yevich Burnazyan--will remain forever in the hearts of all those who knew him.

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